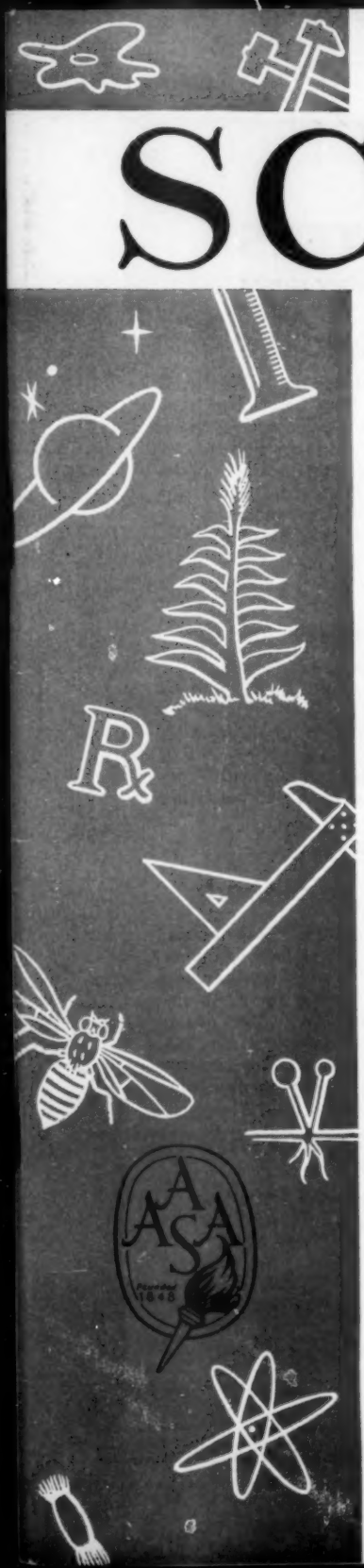

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19 NOVEMBER 1954

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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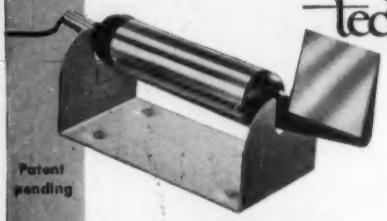

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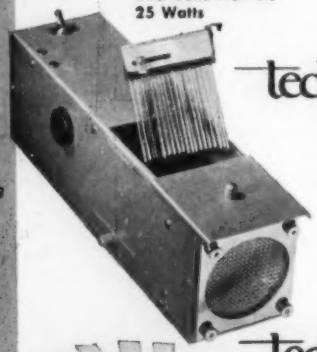

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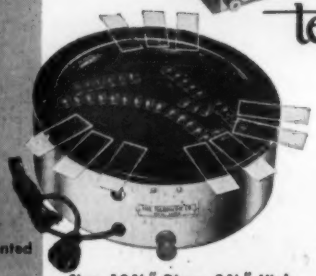

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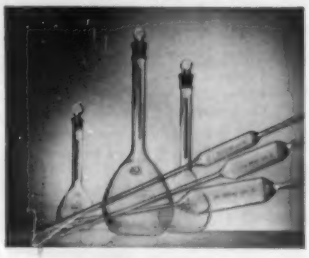

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SLEEPING ACCOMMODATIONS AT 121st AAAS MEETING

Berkeley, California, December 26-31, 1954

The hotel, motel, and dormitory sleeping accommodations—their rates and the application coupon below—are for your convenience in making room reservations in Berkeley. Please send your application *directly* to the AAAS Housing Bureau and thereby avoid delay and confusion. The experienced Bureau will make assignments promptly; a confirmation will be sent you in two weeks or less. **Single rooms may become scarce; double rooms for single occupancy cost more; if possible, share a twin-bedded room with a colleague—and also save.** Mail your application *now* to secure your first choice of desired accommodations. All requests for reservations must give a definite date and estimated hour of arrival and also probable date of departure.

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Other hotels	3.00– 5.00	3.50– 5.00	4.00– 6.50	7.00–10.00

(Note: Most hotels have singles without private bath at $2.00–$3.50 per night)

MOTELS				FAMILY ROOMS
Berkeley Plaza	5.00	6.00	7.00	8.50–12.00
California	4.00– 4.50	4.50– 5.00	5.50	6.00– 7.00
Golden Bear	4.50– 5.00	5.00– 7.00	6.00– 8.00	7.50–10.00
Other motels	4.00– 5.00	4.00– 6.00	5.50– 8.50	6.00–12.00

Dormitory Accommodations: NOTE: The 766 units in the University of California dormitories are primarily for students, younger faculty members, and those not on expense accounts. Occupancy, two persons per room; rate, $2.00 the first night, $1.00 per night thereafter, per person.

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For a discussion of the headquarters of the participating societies and sections, please see Association Affairs, *Science*, July 23, or *The Scientific Monthly*, August.

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Make checks payable to "AAAS Housing Bureau."

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(These must be indicated—add approximate hour, a.m. or p.m.)

NAME .....
(Individual requesting reservation) (please print or type)

ADDRESS .....
(Street) (City and Zone) (State)

My society (or sectional interest) is: .....

I (will) (will not) have an automobile at the Meeting.

Mail this now to the Housing Bureau (address above). *Enclose hotel or motel room deposit. Make checks payable to AAAS HOUSING BUREAU.* **Rooms will be assigned and confirmed in order of receipt of reservation.**

Are the Sciences Too Far Ahead of Advertisers?

The following editorial by C. B. Larrabee in the periodical Printers' Ink *for 22 October brings questions that have long troubled scientists to the attention of the general publishing and advertising fraternities. The use of scientific-sounding but scientifically meaningless or misleading language, distortions of scientific thought and experimental results, false analogies both direct and implied—in short, the misuse of science and scientific evidence—can be found in many fields. It is good to see concrete evidence that others are also concerned with the problem.*

Incidentally, advertising designed to appear in periodicals serving scientists is generally accurate—more informational than promotional. The readers—the potential buyers—help to control the quality of the advertising.

ARE scientists getting ahead of advertising's ability to use their findings wisely?

As few and tentative as are the studies in the field of psychological research, they already have pointed the ways to more skillful manipulation of the consumer mind. The results, therefore, can be as dangerous as they are significant.

For many years advertising has had its unscrupulous fringe. At one time they [unscrupulous advertisers] operated without hindrance. They sold such socially dangerous products as supposed cancer cures and other nostrums. When legislation caught up with them they transferred their activities to other fields.

They began to use the fake testimonial, the pseudo-scientific copy appeal, and all the other petty tricks of the advertising shyster. They have been particularly adept at juggling statistics and backing phony research. . . .

The fact that these people wear the clothes of respectability and wield multi-million-dollar appropriations makes them no less shysters and therefore no less dangerous.

It would be easier not to worry about them. It would be comforting to feel that they will grow up to their responsibilities. But they have never shown that they understand their obligation to society. There is no reason to believe that a scientific refining and sharpening of their tools will suddenly awaken them to their social responsibilities.

The very real possibility that the techniques of social research and psychology will be used by those ill-fitted to use them presents to advertising one of the greatest challenges in its long history.

Advertising has always suffered from those who were so fascinated by the game that they forgot its social implications. As production more and more catches up with capacity to consume, the demand for hard selling will put new premiums on the work of those who understand how to manipulate the human mind.

Somebody once said war is too important to be entrusted to the generals. Is it possible that advertising might become too scientific to be entrusted to advertisers?

Leaders in advertising should see that scientific techniques are not so abused by a few unscrupulous advertisers that their great potential benefits are denied those who can use them wisely and soundly.

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The Gene

L. J. Stadler

University of Missouri and *U.S. Department of Agriculture, Columbia, Missouri*

THE central problem of biology is the physical nature of living substance. It is this that gives drive and zest to the study of the gene, for the investigation of the behavior of genic substance seems at present our most direct approach to this problem.

Current knowledge of the behavior of living cells presents two striking pictures. The first is the almost incredibly delicate balance of chemical reactions occurring in the living cell, by which energy is made available and by which the syntheses proceed that provide the materials for growth. The second is the behavior of the genic substance, which apparently guides these reactions. It is carried in the chromosomes in fine strands, which together make up only a minute portion of the substance of the cell. These strands are differentiated along their length into hundreds of segments of distinctive action, and, therefore, presumably of distinctive constitution, which we speak of as the genes. The genic substance is reduplicated in each cell generation. Its distinctive segments, in many known cases, determine whether or not a specific chemical reaction will occur, presumably, in some cases at least, by determining the production of a specific catalyst.

The great bulk of the substance of the cell apparently consists of materials produced by the aforementioned guided reactions. The nature and behavior of these materials, so far as we know them, do not require the assumption that they have properties essentially different from those of nonliving matter.

The genic substance, on the contrary, appears to have properties quite different from those with which we are familiar from our knowledge of the physical science of nonliving matter. Modern physical science gives us no model to explain the reduplication of the gene-string in each cell generation, or to explain the production of effective quantities of specific enzymes or other agents by specific genes. The precise pairing and interchange of segments by homologous gene-strings at meiosis also suggest novel physical properties of this form of matter. These facts indicate that a knowledge of the nature and properties of the genic substance might give clues to the distinctive physical mechanisms of life.

The difficulties in the study of the genic substance are obvious. It cannot be isolated for chemical analysis or pure culture. The possibility of direct analysis of specific segments or individual genes is, of course, even more remote. The properties of the genes may be inferred only from the results of their action.

Dr. Stadler, before his death on 12 May, asked that this paper be sent to Science. *It is the valediction, and a remarkable one, of a great geneticist.*—EDITORS.

Furthermore, a critical study of the effects of a single gene may be made only by comparing individuals wholly comparable in genotype except for a difference in the one gene concerned. This means that gene mutations are essential for such comparisons, since it is only by gene mutation that we can identify individuals differing only by the effects of a single gene. The prospect of determining the properties of the gene is, therefore, dependent upon the development of valid methods for the study of gene mutation.

It is appropriate to cite here the monumental contributions of H. J. Muller to the investigation of this problem. More than 30 years ago he recognized clearly the unique significance of gene mutation in the study of the physical nature of life (*1*) and boldly attacked the imposing technical problems that blocked its experimental investigation.

The difficulties of analysis that have been mentioned are not different in kind from those involved in other problems in which the properties of hypothetical elements must be inferred from their effects—for example, in the problems of molecular or atomic structure. In such studies, the investigator proceeds by constructing the simplest model that will fit the known facts and then attempting to apply every significant experimental test of the predictions that may be made from the model. By a series of successive approximations, the model finally evolves to a form that seems to provide the most plausible mechanism for the behavior observed. The study of the physical nature of the gene from purely genetic evidence is closely comparable to this.

These difficulties of analysis are mitigated in some degree by the possibility of parallel investigation of certain problems of mutation through direct observation of the chromosomes. Although the gene-string itself is below the limit of microscopic visibility, its behavior is such that it provides a visible shadow, so to speak, in the chromosome. Some alterations of the gene-strings are readily detectable by visible alteration of the chromosomes. The cytogenetic analysis of individual mutations provides a wholesome check on hypotheses derived from the statistics of mutation frequencies.

An illuminating example of this is afforded by certain interpretations of the evidence on mutation rate as affected by x-ray treatment and by temperature. At an early stage in the study of x-ray-induced mutations, Delbrueck (*2*) constructed a tentative "atomic physics model" of the gene, as inferred from the frequency of point mutations observed under varying physical conditions. This has become widely known through its application and discussion in the engaging little book *What Is Life?* (*3*), published several years later by

the eminent theoretical physicist, Erwin Schrödinger.

In this view, the gene is considered a molecule, and the observed mutations are considered to represent its transitions from one stable state to another, as a result of thermal agitation or the absorption of radiant energy. The linear-dosage curve and the constancy of mutation yield, regardless of variation in the time factor, show that the x-ray-induced mutations result from single "hits"; the constant proportionality of mutation yields to ionization, regardless of variation in wavelength, shows that the unit "hit" is an ionization. Calculation of the volume within which these hits must occur to account for the mutations observed provides a basis for estimating the average size of the gene-molecules postulated. This turns out to be of the order of 1000 atoms. The relative frequency of spontaneous mutations at different temperatures permits the calculation of the activation energy required for the occurrence of a mutation, which turns out to be about 1.5 ev. Unstable genes are assumed to have correspondingly lower activation energies, and the fact that temperature affects their mutation rate less than that of normally stable genes is in agreement with expectation on this basis. The energy spent in one ionization is about 30 ev, and it is therefore to be expected that irradiation will cause the mutation of any of the genes, regardless of their relative stability under normal conditions. The proportional increase in mutation rate will, therefore, be much less for genes distinctly unstable at ordinary temperatures than for genes of normal stability. These expectations also are realized.

This is an impressive picture, but it has been evident for many years that it has no valid relationship to the experimental data from which it was derived. The detailed analysis of individual cases among the x-ray-induced mutations has shown clearly that many of these result not from a structural change in a gene but from some alteration external to the gene, such as physical loss or rearrangement of a segment of the gene-string. We have no basis for estimating the proportion of such extragenic mutations among the total of mutations observed and no ground for assuming that this proportion is the same among the mutations observed under the various experimental treatments.

The basis of the model is the assumption that the statistics of observed mutation are in fact the statistics of structural alteration of the molecules that constitute the gene-string. The investigations of specific mutations contradict this assumption and show that the model has no basis in reality.

It is interesting to reflect that if the determiners of heredity had chanced to be of a lower order of magnitude, below the level at which the experimental study of individual cases is possible, we might still be constructing more and more refined models of the gene on this pattern. As the predictions made from the model were contradicted by experimental results, we would change the various numerical values, or introduce additional variables, or perhaps, if necessary, even create additional hypothetical units. But the model would remain essentially an imaginary construct inferred from mere numbers of mutations, for we would have no possibility of contradicting the plausible assumption that one mutation is as good as another.

What Is a Gene?

The early studies of gene mutation were concerned mainly with problems of technique arising from the extreme rarity of the phenomenon. Although the mutations of *Oenothera*, on which the mutation theory was based, had proved illusory, it soon became evident that mutant alterations do occur that are inherited as if they were due to changes in individual genes. The comprehensive genetic analysis of *Drosophila* by Morgan and his coworkers showed numerous cases of this sort—in fact, almost all the loci shown on the gene-map represented the mutant occurrence of visible alterations which, on subsequent tests, proved to be inherited in typical Mendelian fashion. These were assumed to be due, in each case, to a change of the wild-type gene to an alternative form, producing a recognizably different phenotypic effect. The frequency of these mutations, however, seemed far too low to permit experimental investigation of the conditions affecting their occurrence.

Muller (*4*) pointed out in 1917 that gene mutations resulting in inviability ("lethals") are probably more frequent than mutations permitting survival with modified phenotype ("visibles"). In experiments extending over the next 10 years (*5*), he developed various special techniques by which it was possible to determine the total number of lethal mutations for all loci within a given chromosome or region. These total frequencies proved to be high enough to permit significant experimental comparison of mutation frequencies under different temperatures. The loci yielding lethal mutations were distributed over the chromosomes approximately as expected from the distribution of loci for visible mutants, and it was concluded that the lethal mutations might legitimately be used as an index of gene mutations in general.

Meanwhile, many attempts to increase the frequency of genetic alterations by external treatments had been made, including studies with various chemical, radiological, and serological treatments, and studies in which various plant and animal forms were used. None of these experiments gave conclusive proof of an effect of any experimental treatment on the frequency of mutation, although in several of the experiments there were genetic alterations that may have been induced by the treatment. The failure of proof was due to two difficulties: (i) that of proving that the genetic alterations observed in the progeny of treated individuals were in fact due to the treatment rather than to some genetic irregularity present in the treated strains, and (ii) that of showing statistically convincing increases in the frequency of mutations in the treated group. What was needed was a genetic technique suitable for the detection of mutations in adequate numbers in an organism in which the gene-determined inheritance of the mutant characters could be readily demonstrated.

The "C1B" technique with *Drosophila*, designed by

Muller, was admirably suited to this purpose, and x-ray experiments with this technique (*6*, *7*) demonstrated beyond question a very strong effect of x-rays on the frequency of mutation. The total frequency of lethals in the X-chromosome was increased more than 100-fold. In addition, many visible mutations were found, including dominants as well as recessives, and including mutants previously known from their spontaneous occurrence as well as many mutants not previously observed.

These experiments were promptly followed by others designed to test more critically the genic nature of the induced mutations. The mutant lethals might be suspected of being deficiencies; even the visibles could conceivably be due to short deficiency or gene destruction. But if the treatment could induce mutation to a variant allele and could, in further applications, induce reverse mutation to the parental allele, it was argued, the two mutations could not both be due to gene loss. Induced mutation and induced reverse mutation at the same locus were shown to occur in a number of loci of *Drosophila* in experiments by Patterson and Muller (*8*) and by Timoféeff-Ressovsky (*9*).

Subsequent experiments with a wide variety of forms among the higher plants and animals and with microorganisms showed the broad generality of the effects of ionizing radiations upon the frequency of mutation. In later experiments, ultraviolet radiation and various chemical treatments were also shown to affect mutation frequency.

The analysis of the induced mutations, however, soon indicated that the accepted definitions and criterions related to genes and gene mutations needed reconsideration.

The purpose of experiments with gene mutation is to study the evolution of new gene forms. The techniques for studying gene mutation are, therefore, designed to measure the frequency of these changes in the genes. But a change in the gene may be recognized only by its effects, and it soon became clear that various extragenic alterations might produce the effects considered characteristic of typical gene mutation (*10*).

Thus the working definition of mutation necessarily differs from the ideal definition. It is this working definition that must be considered in generalizing from the experimental evidence. The mutations experimentally identified as gene mutations may include not only variations due to alterations within the gene but also variations due to losses of genes, to additions of genes, and to changes in the spatial relationships of genes to one another. To identify these mechanical alterations, certain tests were applicable. But there was no test to identify mutations due to a change within the gene; it was simply inferred that the mutants that could not be identified as the result of specific mechanical causes were, in fact, due to gene mutation in the ideal sense (*11*).

When we conclude from an experiment that new genes have been evolved by the action of x-rays, we are not simply stating the results of the experiment. We are, in the single statement, combining two distinct steps: (i) stating the observed results of the experiment, and (ii) interpreting the mutations as due to a specific mechanism. It is essential that these two steps be kept separate, because the first step represents a permanent addition to the known body of fact, whereas the second step represents only an inference that may later be modified or contradicted by additional facts. When the two steps are unconsciously combined, we risk confusing what we know with what we only think we know.

The widely held belief that the frequency of gene mutation may be greatly accelerated by x-ray treatment was an illusion of this kind. Its basis was the use of the term *gene mutation* with two distinctly different meanings. Gene mutation was thought of as a change in the constitution of a unit of the genetic material, producing a new gene with altered gene action. Gene mutation was identified in experiments by the occurrence of a mutant character inherited as if it were due to a change in a gene.

The mischief involved in the use of the same term for the two concepts is obvious. To insist that x-rays induce gene mutation because the mutants induced saitsfy all the accepted criterions of gene mutation, and that these mutants represent qualitative changes in specific genes because that is what we mean by gene mutation, is to adopt the dictum of Humpty Dumpty in *Through the Looking-Glass*. "When I use a word," Humpty Dumpty said, "it means just what I choose it to mean—neither more nor less."

Now our concept of the gene is entirely dependent upon the occurrence of gene mutations. If there were no gene mutations, we could not identify individual genes, because the total genetic effect of a single chromosome would be inherited as a unit. If the mutations we interpret as gene mutations are in fact due to alterations affecting groups of genes, then the entities that we will recognize as genes will be in fact the corresponding groups of genes. The significant ambiguity is not in our definition of gene mutation but in our definition of the gene itself, because any definition of gene mutation presupposes a definition of the gene.

The discussion of these difficulties and of the possibility of remedying them by more rigorous definition of experimental concepts is only an application to biology of the operational viewpoint that has become commonplace in modern physics, largely as a result of the critical studies of P. W. Bridgman (*12*). As Bridgman notes, this sort of critical reconsideration, made necessary in physics by the development of relativity, is essential in scientific thinking if the methods are to be made elastic enough to deal with any sort of facts that may develop. The essential feature of the operational viewpoint is that an object or phenomenon under experimental investigation cannot usefully be defined in terms of assumed properties beyond experimental determination but rather must be defined in terms of the actual operations that may be applied in dealing with it. The principle is not a new one; it has

been recognized, at least implicitly, in the work of individual scientists from an early period. William James stated it essentially in his lectures on pragmatism (*13*), illustrating it with a quotation from Wilhelm Ostwald:

> Chemists have long wrangled over the inner constitution of certain bodies called tautomerous. Their properties seemed equally consistent with the notion that an instable hydrogen atom oscillates inside of them, or that they are instable mixtures of two bodies. Controversy raged but never was decided. "It would never have begun," says Ostwald, "if the combatants had asked themselves what particular experimental fact could have been made different by one or the other view being correct. For it would then have appeared that no difference of fact could possibly ensue; and the quarrel was as unreal as if, theorizing in primitive times about the raising of dough by yeast, one party should have invoked a 'brownie' while another insisted on an 'elf' as the true cause of the phenomenon."

What is a gene in operational terms? In other words, how can we define the gene in such a way as to separate established fact from inference and interpretation? The definition may take into account not merely the evidence from experiments on the occurrence of mutations but also the evidence from experiments on the inheritance of genetic differences of any kind, or from any other experiments that bear on the nature of the gene. The definition may specify attributes of the gene that can be determined by recognized experimental operations, whether these are attributes already established in past experiments or attributes that might be determined in future experiments.

Operationally, the gene can be defined only as the smallest segment of the gene-string that can be shown to be consistently associated with the occurrence of a specific genetic effect. It cannot be defined as a single molecule, because we have no experimental operations that can be applied in actual cases to determine whether or not a given gene is a single molecule. It cannot be defined as an indivisible unit, because, although our definition provides that we will recognize as separate genes any determiners actually separated by crossing over or translocation, there is no experimental operation that can prove that further separation is impossible. For similar reasons, it cannot be defined as the unit of reproduction or the unit of action of the gene-string, nor can it be shown to be delimited from neighboring genes by definite boundaries.

This does not mean that questions concerning the undetermined properties mentioned are meaningless questions. On the contrary, they are the all-important questions that we hope ultimately to answer by the interpretation of the experimental evidence and by the development of new experimental operations. The operational definition merely represents the properties of the actual gene, so far as they may be established from experimental evidence by present methods. The inferences from this evidence provide a tentative model of the hypothetical gene, a model that will be somewhat different in the minds of different students of the problem and will be further modified in the light of further investigation.

The term *gene* as used in current genetic literature means sometimes the operational gene and sometimes the hypothetical gene, and sometimes, it must be confessed, a curious conglomeration of the two. The resulting confusion may be strikingly illustrated in seemingly contradictory statements by two such gifted and clear-sighted geneticists as Richard Goldschmidt and A. H. Sturtevant. Goldschmidt, after reviewing the evidence on position effect, states that genes do not exist (*14*), or at any rate that the classical theory of the corpuscular gene must be discarded (*15*). Sturtevant, citing the evidence that chromosomes are regionally differentiated, that particular regions are necessary for particular reactions in the organism, and that these particular regions behave as units in crossing over, states "These propositions . . . prove the existence of genes" (*16*).

Goldschmidt is essentially correct if, by the gene, we mean the hypothetical gene, and the particular hypothetical gene that he has in mind. His positive conclusion that the gene does not exist is prone to misinterpretation but apparently means only that this hypothetical gene does not exist. His contention that the properties commonly ascribed to "the classical, corpuscular gene" go far beyond the evidence is, I think, fully justified.

Sturtevant is correct if, by the gene, we mean the gene of the operational definition, since this implies no unproved properties. If it were true that there are no discrete units in the gene-string, Sturtevant points out, the most direct way of establishing the fact experimentally would still be by studying the properties and interrelationships of these distinguishable regions. These are the genes of the operational definition.

What is the operational definition of gene mutation? We have recognized that our studies of gene mutation have significance for the major problem only to the extent that they identify and analyze the mutations that represent the evolution of new hereditary units. But it is obvious that no operational definition of gene mutation in this sense can now be formulated—for these hereditary units are not the genes of the operational definition; they are the hypothetical genes postulated in our interpretation of the experimental evidence. To say that no operational definition is now possible is only to repeat in different words the foregoing statement that we have no positive criterion to identify mutations caused by a change within the gene, and that the alterations interpreted as gene mutations in experiments are merely the unclassified residue that cannot be proved to be due to other causes. The major objective in further investigations must be to develop such criterions.

Study of the Mutation of Specific Genes

The main purpose of this paper (*17*) is to emphasize the unpleasant fact that significant progress in our understanding of gene mutation requires the investigation of the mutation of specific genes. The fact is unpleasant because the various technical difficulties

that arise from the very low frequency characteristic of mutation are at their worst when the study must be made on single genes, particularly on the spontaneous mutation of single genes. The unpleasant statement is a fact because, as we have seen, it is hopeless to identify and exclude the spurious or extragenic mutations in experiments on mutation rates at miscellaneous unspecified loci.

The chief advantage in focusing the study on the single gene is that this makes it possible to substitute the direct experimental analysis of specific mutants for the application of generalizations assumed to apply to mutations at all loci. Each mutant studied may add to the background of detailed information available for the diagnosis of other mutants of the same gene.

An important further advantage is that the specific loci selected for study may be loci with unusual technical advantages for the recognition and analysis of their mutants. For example, the genes R^r and A^1 in maize, like other known genes in various species, yield spontaneous mutants that are clearly distinct from the forms produced by recognizable short deficiencies at these loci. This does not prove that the spontaneous mutants are not due to still smaller deficiencies, but it supplies a convenient screen for identifying a large class of deficiencies without further investigation. Another very useful aid in discriminating between gene loss and gene alteration is available for the recessive allele *a*. This allele, although phenotypically distinguishable only by the loss of *A* action, may be distinguished from gene deficiency by its response to the mutagenic gene Dotted (*Dt*), in the presence of which it reverts sporadically to the dominant allele *A*. The retention of the *Dt* response provides a criterion to exclude gene loss in the interpretation of experiments on spontaneous and induced mutation of *A*. A technical advantage of a different sort is provided by the *R* alleles. The phenotypic effect of *R* is such that a large number of alleles may be objectively distinguished by very slight differences of plant color intensity and pattern. A gene with equally variable allelic forms, if identified only by its effect on some all-or-none response, would seem to have only two alleles, and its mutations would not be detectable except for those that crossed the line between these two distinguishable levels of action. Another advantage of great practical importance is that both *R* and *A* are genes affecting endosperm characters and are, therefore, suitable for the identification of mutations in large populations. Both are apparently genes of such trivial effect physiologically that their mutants survive with no detectable loss of viability.

The effective analysis of the diverse genetic phenomena that may result in the origin of a Mendelizing variation may not be impossible in intensive studies of the mutations of suitable selected genes, despite the fact that it seems hopeless in studies of mutation at miscellaneous, unspecified loci.

These considerations are of no account if the frequency of spontaneous mutation of the single gene is actually too low to permit effective experimental study. We cannot safely avoid this difficulty by selecting for study the genes of unusually high mutation frequency, because there is no assurance that the mechanism responsible for the behavior of "unstable genes" is representative of the mechanisms concerned in typical gene mutation. The use of microorganisms that permit effective screening for mutants in virtually unlimited populations would remove the difficulty, but unfortunately these do not provide the critical genetic background essential to the study.

A technique for determining the spontaneous frequency of mutation of specific genes is practicable in maize for mutation rates ranging as low as about one per 1 million gametes (*18*). A test of eight genes, unselected except for the technical advantage of showing their effects in the endosperm, yielded mutations in all but one of the genes tested, the mutation frequencies ranging from about one to about 500 per 1 million gametes tested (*19*). The genes that yielded mutations in sufficient numbers to permit the comparisons showed rather wide variation in mutation frequency in different cultures. The gene *R*, for example, yielded no mutations in large populations in some cultures, but its mutation rate in other cultures ranged as high as 0.2 percent. Later studies have shown that such differences are due in part to differences intrinsic to the *R* allele concerned and in part to differences caused by factors modifying the mutation rate of R (*20*). Such factors are apparently quite common, since a study in which only strong effects could be detected indicated the occurrence of such modifiers in three of the seven regions marked (*21*).

The average mutation rates determined are rather low for effective experimental investigation of factors affecting the mutation rate and even for the extraction of adequate samples of mutants for individual study. However, the fact that mutation rates are so readily affected by diverse modifiers makes it feasible to extract strains in which the mutations of specific genes may be made frequent enough to permit direct experimenal study.

Detection of Spurious Gene Mutations

The development of criterions for identifying gene mutations of evolutionary significance is difficult even in the study of selected genes of the most favorable properties. In past studies, the problem has been given a disarmingly simple appearance by various assumptions, some of which were unwarranted, and some of which have been invalidated by later discoveries.

For example, we tend to feel that some of the mutations detected in our experiments must be qualitative changes in the genes concerned, for surely qualitatively altered genes have arisen in the course of evolution. This is mainly responsible for the widespread belief that, even though some of the apparent gene mutations identified are demonstrably false, "true" gene mutations must be included in the unclassified residue.

This belief is fallacious. Granting that qualitatively changed genes must have been evolved by mutation at rates high enough to permit experimental investiga-

tion, there is no assurance that the steps in their evolution are represented in the mutants that are found in our mutation experiments. When we set out to identify mutants in a mutation experiment, we must confine ourselves to mutations of relatively large effect, large enough to set the mutant beyond the range of varying expression due to environmental and genetic modifiers. If mutant changes occur within the narrower range, we have no way of identifying them. There is no good evidence against the occurrence of such subliminal mutations. The assumption of the high constancy of the gene is backed by evidence only concerning the rarity of the distinct mutations. If convincing evidence were adduced tomorrow to show that genotypes breed true only as a statistical result of sampling in each generation in populations of genes genetically fluctuating over an imperceptible range, there is nothing in our present knowledge that would contradict this conclusion.

A study of *R* alleles of diverse origin showed the common occurrence of minute differences in the level of plant-color expression (*22*). Such allelic differences would not be expected if the only source of variation in this gene were mutation of the type that we study in our experiments, but they would be expected as a result of subliminal mutation.

If subliminal mutations occur, it is possible that this type of mutation accounts largely or wholly for the evolution of new gene forms in nature. Thus it is quite possible that the sharply distinct mutations identified in our experiments may be exclusively the result of extragenic phenomena.

A second assumption, or group of assumptions, is concerned with the possibility of distinguishing gene mutation from gene loss. It was originally supposed that induced recessive "visibles" could safely be considered gene mutations, on the assumption that all genes were essential to survival. This was contradicted by various instances of cytologically demonstrable deficiencies viable in haploid tissue or in hemizygous individuals, or viable as homozygotes in diploid individuals. Such cases were relatively few, but since both the cytological and the genetic criterions of deficiency approach the limit of their range of effective application as the deficient segment becomes smaller, there is reason to suspect that physical loss may be responsible for observed mutations also in cases in which deficiency cannot be demonstrated. As we have become better acquainted with individual genes and their functions, the assumption that genes, as a rule, are individually essential to life has lost its plausibility.

Mutation to an intermediate allele is sometimes considered evidence against loss mutation. This involves another assumption, that of the unitary nature of the gene—an assumption made consciously and with careful consideration in the early development of gene theory, but one that must be seriously questioned in the light of later evidence. It is only on the hypothesis that multiple alleles are variant forms of a single unit that we may exclude the possibility of their occurrence by loss mutation. On the hypothesis that they represent different mutations in a complex of closely linked genes, we could account for mutation to different levels by the loss of different segments of the chain.

The basis for the choice of the unitary hypothesis is perhaps best shown in the considerations underlying the classical criterion of allelism. These were stated by Morgan in 1919 (*23*) as follows:

> Probably the most important evidence bearing on the nature of the genes is that derived from multiple allelomorphs. Now that proof has been furnished that the phenomena connected with these cases are not due to nests of closely linked genes, we can probably appeal to these as crucial cases. . . . The demonstration that multiple allelomorphs are modifications of the same locus in the chromosome, rather than cases of closely linked genes, can come only where their origin is known. . . .

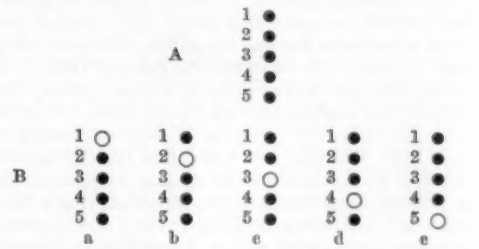


Fig. 108 [in part]. Diagram illustrating mutation in a nest of genes so closely linked that no crossing over takes place.

> Let the five circles of Fig. 108, *A* represent a *nest* of closely linked genes. If a recessive mutation occurs in the first one (line *B*, *a*) and another in the second gene (line *B*, *b*), the two mutants *a* and *b* if crossed should give the atavistic type, since *a* brings in the normal allelomorph (*B*) of *b*, and *b* that (*A*) of *a*. . . . Now this is exactly what does *not* take place when members of an allelomorphic series are crossed —they do not give the wild type, but one of the other mutant types or an intermediate character. Evidently independent mutation in a nest of linked normal genes will not explain the results if the new genes arise directly each from a different normal allelomorph.

It will be noted that the test rules out the existence of the nest of closely linked genes only on the assumption that each mutation must be an alteration of a single number of the group. If, instead, each mutation were a loss of one or more contiguous numbers of the group, the fact that crosses between them might commonly show them to be allelic would not rule out the "compound gene" as the basis of the multiple allelic series. This is illustrated in the following diagrammatic arrangement:

1 ●	1 ●	1 —	1 ●	1 ●
2 —	2 ●	2 —	2 ●	2 ●
3 —	3 —	3 —	3 —	3 —
4 ●	4 —	4 —	4 ●	4 —
5 ●	5 —	5 ●	5 ●	5 —

The "compound gene" is in a sense a contradiction in terms, for the hypothetical gene is unitary by defi-

nition. But the genes identified in our experiments cannot be made unitary by definition. The five genic elements represented in the diagram are not actually parts of one gene; they are five genes. But if certain multiple allelic series have a basis of this type, it would be possible to establish the fact experimentally only in the cases most favorable for analysis. Accordingly, there might be many cases in which the segment of the gene-string identified experimentally as a single gene might actually be a cluster of genes of identical or similar effect.

The notion of the compound gene, or some equivalent unit, may prove to have significance, since there may be special relationships among the clustered elements that mark them off as a group from adjoining unrelated elements. One of these may be interrelationships in gene action between the clustered elements, which could lead to the occurrence of position effects when members of the cluster are separated by crossing over or translocation. This may be a basic factor in the explanation of position effect in general. Another relationship to be expected is synaptic equivalence, leading to the opportunity of unequal crossing over. It is the latter that concerns us here.

A striking example of minute deficiencies simulating gene mutations is provided by the "crossover-mutants" of R^r (*24*). Certain R^r alleles consist of at least two independently mutating genic elements: (P), determining anthocyanin pigmentation of certain plant tissues and of the pericarp, and (S), determining anthocyanin pigmentation of the endosperm and embryo. The crossover-mutants R^g and r^r result from unequal crossing over and must, therefore, involve the loss of (P) in the one case and of (S) in the other. They give no cytological or genetic indication of deficiency, and they are wholly normal in development in the haploid gametophyte, as is shown even by the very sensitive test of competitive pollen-tube growth in the transmission of the mutant through male germ cells. The crossover-mutants are wholly indistinguishable in appearance and genetic behavior from the noncrossover mutants occurring in the same cultures.

The occurrence of unequal crossing over within the *R* complex yields some interesting indications of the genetic nature of multiple allelic series and of the possible role of gene losses in relation to seemingly qualitative mutations. In addition to (P) and (S), there are other phenotypically recognizable genic elements of the *R* complex. In certain R^r alleles of dilute pigmentation, both plant and seed color are dependent upon a single genic element (D). In various R^r alleles of unusually strong pigmentation, there appear to be additional elements determining certain aspects of plant-color expression. In addition, there are various distinguishable aleurone-color types such as "Stippled," "Marbled," "Navajo-spot," and so forth, some occurring with plant color and some without. Each of the distinguishable complexes may be regarded as one of a long series of multiple alleles of the gene *R*.

Let us pause a moment to clear the terminology. To avoid confusion I shall refer to the recognized alleles of *R* under their customary italicized designations (R^r, R^g, r^r, R^{Nj}, and so forth), although the analysis shows that several of these so-called "alleles" are actually complexes of two or more genes.

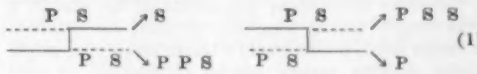
The term *genic element* will be used for any gene-like constituent identified as a component of one of the *R* alleles. The use of this term does not, in the absence of further evidence, necessarily imply that the element is unitary. The genic elements are designated by symbols not italicized, such as P, S, D, and so forth.

In addition to the crossover mutants there are numerous noncrossover mutants. A noncrossover r^r mutant is presumably of constitution "P s" rather than merely "P." The postulated element (s) is a "null" element phenotypically but presumably would function synaptically in the same way as "S." These postulated elements are designated "s," "p," "d," and so forth.

The complex may, of course, include other null elements from past mutations in which the parental elements are unknown. These as a class are designated as "n."

In several instances noncrossover mutants to intermediate levels of seed-color expression occurred including various dilution and pattern types. These are designated "S^d," "S^i," and so forth.

Once any two of these genic elements have become established in neighboring positions in the same chromosome, an opportunity is provided for unequal crossing over, which may ultimately lead to the development of more complex gene clusters. For example, the aforementioned crossover mutants resulted from interchanges as follows:



The crossover-product "S" was recognizable as a crossover mutant R^g and the crossover-product "P" as crossover mutant r^r. The crossover-products "P P S" and "P S S" were not recognizable, but these represented the production of potential new alleles carrying three genic elements instead of two. By using distinguishable forms of S or P in the original compound, the addition-crossovers may be made recognizable, and by this means it is possible to produce such new synthetic alleles as *R* (Stippled-Navajo), and so forth. In this manner, it would be expected that more complex clusters would develop by successive steps, unless the gene is one whose action sets a closer limit on the viability of its duplications.

The great variety of genotypes that might be expected to represent possible members of the allelic series may be illustrated by a few examples as follows:

1) S S p n
2) S P P n S
3) D
4) D S P
5) S^i P D

Alleles (2) and (4) would be of the standard R^r type, (3) would be of the dilute R^r type, (1) would be of the

R^g type, and (5) would be a spotted aleurone type with plant color. In general, the differences between the alleles are due to extragenic, rather than intragenic, alterations, but this is not necessarily true of the phenotypic difference between (4) and (5).

With regard to the relationships between the genic elements of the complex, the concepts of allelism and locus have little meaning. All members of the complex are homologous with one another; presumably all have arisen through a long series of mutations from some single ancestral gene. In a sense, all may be considered allelic to one another. For example, the question "Is S^n (the seed-color element in R^{NJ}) allele to S?" has no significance, because there is no way in which S^n can be shown to have any different relationship to S than to P or to any other element of the complex. The same is true of such a question as "Is the element (D) proximal or distal to (P)?" It may be proximal in one stock and distal in another; in a stock in which it is proximal, a short series of unequal crossovers will suffice to move it to a distal position.

Although different alleles may have widely different numbers of genic elements, none is actually a deficiency. In terms of the postulated origin of the cluster, all of those with more than a single element may be considered duplications. On the other hand, when we arbitrarily take as the standard type an allele carrying several genic elements, other alleles with fewer elements will appear as deficiencies, and the mechanisms that produce them as mutants from the standard type will be mechanisms of gene loss.

The same mechanisms proceeding in the case of a gene-complex whose separable elements are identical in action might produce only a linear series of multiple alleles showing various grades of dilution, or they might produce no multiple series of alleles at all.

The increasing number of cases in which clustering of genes of identical or similar effect is proved or indicated (*24–27* and others, *28* and *29* for references) suggests that unequal crossing over may be a significant factor in the production of seemingly qualitative allelic differences.

Another simplifying assumption was that mutant changes in gene effect must represent some transformation of the gene itself rather than some alteration affecting its expression. It was this assumption that made the demonstration of x-ray-induced mutation and reversion of the same gene seem critical proof of the induction of intragenic alterations. The assumption was definitely contradicted by the evidence of position effect. This evidence showed conclusively that a mutation did not necessarily represent a transformation or loss of the gene concerned; instead, it could be the result of a translocation affecting the expression of the unchanged gene.

The remarkable studies of McClintock (*30, 31*) on mutational behavior in maize, as affected by the introduction of a chromosome-9 undergoing the breakage-fusion-bridge cycle, have shown the far-reaching importance of this limitation in the experimental study of gene mutation. In the presence of this structurally unstable chromosome, many of the type genes present, including genes in chromosome-9 and genes in other chromosomes, show mutation to unstable recessive forms characterized by various types of chromosomal irregularity. The study of the unstable mutants and their reversion leaves little doubt that the phenomenon is due to some reversible inhibition of the expression of the genes concerned.

In some cases the mutations are accompanied by detectable chromosomal aberrations at or near the locus showing instability, but in other cases no cytologically detectable chromosomal alteration is associated with the occurrence of the mutation. In many cases the instability of the recessive mutant and the occurrence of the associated chromosomal irregularities are dependent upon the presence of a complementary factor designated "activator" (Ac), and when this factor is removed the mutant behaves as a stable recessive with normal chromosomal behavior.

McClintock has also shown that the control of reverse mutation of the recessive *a* by *Dt* (Dotted) may be a reaction of the activator type. In the presence of the aberrant chromosome-9 and in the absence of *Dt*, the standard *a* allele has given occasional endosperm dots apparently due to mutation to *A*. This strongly indicates that the standard *a* is a repressed *A*, and, if so, its reversion under the influence of *Dt* must also be due to some modification of conditions affecting gene expression.

Whether or not there is acceptance of my hypothesis that these manifestations of unstable gene behavior are brought about by the transposition of invisible bits of heterochromatin to the locus of the gene affected, this brilliant investigation clearly shows that expression effects may be the actual cause of apparent gene mutations, even when the mutation observed shows no indication of a change of position or of any associated chromosomal alteration.

The resulting difficulty in the analysis of observed mutations further emphasizes the necessity for carrying on the analysis with the advantages of the detailed study of mutation at specific loci. If we think of these results in terms of the generalizing assumptions characteristic of the study of mutation *en masse*, we may be inclined to apply the findings to the nature of gene instability in general, or even to the nature of mutant alleles in general. If we think of them against the background of diverse mutations of some intensively studied gene, we are inclined to make detailed comparisons of the mutants of this category with those of other types and other modes of origin in the hope of developing criterions that distinguish mutants of different kinds.

Meanwhile, in the study of gene mutation, we are for the present in an anomalous position. A mutant may meet every test of gene mutation, and yet, if it is not capable of reverse mutation there is ground for the suspicion that it may be due to gene loss, while, if it is capable of reverse mutation, there is ground for the suspicion that it may be due to an expression-effect. The only escape from this dilemma is through the more

intensive study of the mutations of specific genes selected as best suited to detailed genetic analysis, in the hope of developing more sensitive criterions for the identification of gene mutations.

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Erosion Phenomena

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THERE are a number of interesting erosion phenomena that are not the result of an equilibrium between heat exchange by radiation and by convection, yet the effects are in some cases so similar to such equilibrium effects that at first glance these erosion phenomena appear to belong in the same class.

Fluted rocks. In many mountain regions one finds very striking erosion phenomena in limestone: well-formed channels leading downhill. Their bottom is invariably rounded, and the ridges between the channels are exceedingly sharp. These channels vary in width from a fraction of an inch to several feet, and their length may easily attain 30 ft. On the side walls of the larger channels new, smaller channels are formed. They too lead in the direction of maximum inclination. They are undoubtedly formed by rain water containing, of course, carbon dioxide.

The explanation is a very old and simple one: If a slightly inclined rock surface, probably originally polished by glacier action, is not perfectly flat, then after each rain the deeper places will remain wet longer than the protruding parts. At these places the erosion proceeds faster than at elevated, drier regions. The differences between high and low are, therefore, accentuated by rain water. The edges between two channels get more and more elevated above the deeper parts of the rock and, after each rain, they are the first to dry. These ridges between the channels get sharper and sharper, and they can, without exaggeration, be compared to knife edges. At some places the water seems to have found a vertical crack, and these cracks are then widened to deep crevasses, which may have a width of several feet. It is well known in such mountain regions that sheep can be killed when they fall into these holes.

Similar formations can be observed in gypsum rocks. I have climbed, with the aid of a rope, down into some of these vertical shafts, which had a perfectly circular cross section and the walls of which were quite smooth. These "chimneys" in gypsum rocks are harder to explain, but they may well be related to the better known fluted rocks in limestone.

Action of acid on files. It is well known that if a dull file is dipped for a few minutes into concentrated hydrochloric acid, it will come out considerably sharper than it was before the dipping. This phenomenon is very similar to the formation of fluted rocks, but it is more difficult to explain because there is no reason why the action of the acid should be less strong on the ridges than on the grooves. Here we apparently need a geometric explanation.

Let us assume that we start with an iron plate that is fluted with alternating convex and concave cylinder surfaces, all of the same radius of curvature. If the acid acts with the same speed on the ridges and on the grooves, the radius of curvature of the grooves will increase until the concave cylindrical surfaces of the grooves meet, whereas the radius of curvature of the ridges will decrease. When these radii have reached a zero value, the grooves meet and a maximum sharpness of the ridges is attained. From then on any further

action of the acid will produce no further improvement of the file but will produce a gradually progressing deterioration. The radius of curvature of the convex areas remains zero indefinitely, but the angle at which the concave areas meet gradually approaches 180°. This gradual "resmoothing" of the file is in sharp contrast to the formation of fluted rocks which, as years or centuries pass, always progresses, never recedes. The ridges on the file, in contradistinction to the ridges on the fluted rocks, are exposed to the action of the acid for the same length of time as the grooves.

"Dish formation" in old avalanche snow. When, during the winter, an avalanche has come down a mountain slope it frequently remains strongly compacted in the bed of a small creek for a considerable part of the following summer. In this case it is likely that the creek will again find its way along the bottom of its old bed, deep under the old avalanche snow. Soon warm air, too, will find its way along the water and will form a tunnel under the avalanche. When this tunnel is open at both ends of the snow field a considerable air flow takes place downward through this tunnel whenever the temperature of the outside atmospheric air is above freezing. This air drift produces a rapid melting of the old snow, and toward the middle of the summer a sizable tunnel has been formed. Tunnels of this sort are frequently 5 to 10 ft high, and it is easy to follow the creek for considerable distances under the snow mass.

It is quite evident that under these conditions the melting is done entirely or almost entirely by the flow of warm air. The sun never reaches the ceiling of these caves, and the radiation by the bottom of the cave which itself is near freezing, seems to be negligible.

"Dish formation" on remnant of old avalanche, Simplon Pass, Switzerland, May 1954.

Under the described conditions we invariably see a very striking phenomenon on the ceiling of the cave as well as on the walls. The whole surface of the snow is composed of a multitude of concave spherical surfaces or "dishes" forming sharp ridges at the place where two of these surfaces meet. The borderline of each dish is, therefore, polygonal. The dishes often reach 1 ft in diameter. There is little doubt that these ridges are formed in the same manner as the sharp ridges of the old file dipped into hydrochloric acid. It is, however, rather surprising that the phenomenon does not come to an end. Apparently there are always enough irregularities in the snow to prevent the theoretically possible formation of an entirely smooth surface. It may be noted that the formation of dishes is not confined to the inside of the caves; it is also seen, although less well pronounced, on the upper surface of the snow field.

Sophia H. Eckerson, Plant Microchemist

FOLLOWING a week's illness, Sophia Hennion Eckerson, retired plant microchemist at Boyce Thompson Institute for Plant Research, died on 19 July 1954. Born in Old Tappan, N. J., Dr. Eckerson had an inheritance of old Dutch and French blood from her parents, Albert Bogert and Ann (Hennion) Eckerson.

Entering Smith College as a mature student, after helping younger brothers establish themselves in their chosen fields of medicine and art, she received her A.B. degree in 1905 and her A.M. degree in 1907. In 1911, she received her Ph.D. at the University of Chicago, where she continued on the staff until 1920, although the school was not then noted for its liberal attitude toward women on its scientific staff. Her ability as a microchemist led to appointment under that title for a term at Washington State College in 1914; with the Bureau of Plant Industry, USDA, Washington, D.C., 1919; with Cereals Division, 1921–22; with the University of Wisconsin, 1921–23. Becoming plant microchemist at Boyce Thompson Institute when it was organized in 1924, she continued in this position until retirement in 1940.

A versatile person with wide interest in letters and art as well as science, Dr. Eckerson showed the effect of her early training in plant physiology with William Francis Ganong, an outstanding teacher. Her earliest publications are cited in the second edition of *The Teaching Botanist*, which he was then preparing. Throughout her life, she influenced young scientists, whether as aspirants for the doctoral degree, with a thesis to develop and write, or as members of formal classes or informal groups, organized to take advantage of her ability to teach them the special methods she had developed for following metabolic processes in plants by detection of the products through crystallization or by color reactions. Indeed her many students used the mimeographed copies of her "Outlines of plant microchemistry" as a class textbook, so that although she was too much of a perfectionist to publish the last draft of a book designed for class use, her methods have been widely disseminated and incorporated into the textbooks of others.

Throughout her career, she gave generously and enthusiastically of her time and experience to many in organizing and pursuing botanical problems as well as

in the careful presentation of the finished work. The list of her publications gives evidence of her wide interests—in such diverse special fields as microchemistry, germination, mineral nutrition, reduction of nitrates by plants, nitrate reducase, cell walls, endophytic fungi, starch grains. Possibly outstanding in their effect are "Microchemical studies of the progressive development of the wheat plant," "A physiological and chemical study of after-ripening," and her contributions on the structure of cellulose membranes and starch grains.

Never a "joiner," she nevertheless gave good support to Sigma Delta Epsilon in its youthful days. Her academic standing was evidenced by membership in Phi Beta Kappa and Sigma Xi, and the esteem in which her fellow-botanists held her resulted in election to the chairmanship of the Physiological Section of the Botanical Society of America, a rare position for a woman. Her name was in the starred list of outstanding scientists in *American Men of Science* in 1938. Quite outside of organizations, a host of former students and associates feel the loss of the quiet, reserved friend who spent her last years of retirement with her hobbies of reading, handwork, and a real garden in Pleasant Valley, Connecticut.

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News and Notes

Botanical Congress in Paris

An exceptionally cool summer provided an excellent atmosphere for the sessions of the 8th International Botanical Congress in Paris, 2–14 July. Almost 3000 participants were registered. Several special sessions preceded the general meetings. One was that of the Nomenclature Commission, which spent several days in stormy discussion of proposed amendments. A very controversial item was the always resurgent *nomina specifica conservanda*. The good humor of the chairman, Jacques Rousseau (Montreal), rescued the proceedings from pandemonium many times. Another initiative was a "colloque" (symposium) on the "ecological divisions of the world." This, like all such undertakings, was very uneven in content, coverage, and level. The French schools (Toulouse and Montpellier) gave a brilliant account of their methods and their achievements. An exhibition of maps was held concurrently, which showed the excellent work in the past 15 yr of Gaussen (Toulouse) and his collaborators. Other exhibits were by Hueck (São Paulo), Küchler (Kansas), Tüxen (Stolzenau), and Schmid (Zürich).

After the official opening of the congress on 2 July, the participants in the preliminary meetings joined one or another of the 37 sections in which symposiums and miscellaneous papers were being presented. The program was very full and all sections were well attended. As at all such meetings, much time was unavoidably wasted in walking from one section to another and much frustration was experienced because of time conflicts. It is unfortunate that the time restriction for each paper cannot be enforced, but perhaps this requires more fortitude than section chairmen are able to muster. It is, of course, quite impossible to give an account, section by section, of the proceedings and to cite even the most interesting features in each one. I have, however, obtained the collaboration of my colleagues, W. Randolph Taylor, Rogers McVaugh, Chester A. Arnold, and Volney H. Jones, who, respectively, provided notes on phycology, taxonomy, paleobotany, and ethnobotany, whereas I attended the ecology, phytosociology, and protection of nature sections myself. This coverage leaves much that is of equal importance unmentioned.

Phycology. The section of phycology held 17 of the scheduled 18 sessions. One joint session with geology was eliminated because of the death of F. E. Fritsch and the absence of the other chief phycological speaker. About 10 unscheduled papers were added to the program, so that the total of papers was about 120, but several were omitted because of absence of the authors. The attendance varied from 30 persons to 90 or 100 but averaged more than 50 at all times.

The subjects that attracted the most contributors dealt with phytogeography and marine ecology, the vegetation of Africa having been especially favored. A meeting on this last brought together several people long interested in African algae and resulted in an important contribution on the structure of cilia by I. Manton of Leeds. This paper, with the balance of the program, led to very active discussion. So did the program on life-cycles of algae, opened by K. M. Drew Baker, in which various opposing viewpoints were vigorously presented. Programs previously initiated at Stockholm dealing with electron-microscopic structure of diatom cell walls were extended at Paris to other diatoms and to Coccolithophondae, showing astonishing degrees of submicroscopic complexity. The section dealing with biochemistry of marine algae was opened by F. N. Woodward and was an exceedingly crowded one. Although the field was outside the competence of most of the members of the section, the attendance was large and the discussion, especially from visiting physiologists, was as active as the limited time permitted.

In the section dealing with cytology of algae the remarkable studies on chromosome number of *Spirogyra* by Godward were extended and, as indicated by a first communication by C. G. King, desmids have been added to the algal groups that are being inten-

sively investigated. The summary of the ecology of marine phytoplankton by T. Braarud attracted a good deal of discussion. Freshwater algae came in for their share of attention, but the offerings were not as varied as those on marine algae. The chief papers dealt with flagellate organisms and matters of structure and relationships; there were few floristic papers. Among the more considerable studies were those on stream algae by Symoens and on East African lakes by R. Ross. Given the attendance record and the varied program, the continuance of the section for the Montreal meeting seems highly advisable.

Taxonomy. The nomenclature section held its meetings from 28 June to 1 July. Principal business was the consideration of proposed changes in the International Code of Botanical Nomenclature. No major changes were approved; a summary of the actions taken by this section has appeared in *Taxon* 3, 184 (Sept. 1954).

Probably the most important action taken by the section of taxonomy, systematics, and phylogeny was the approval of a resolution to prepare in the near future an *Index nominum genericorum*—a general index of all published genera of plants—and the appointment of an international advisory committee headed by J. Lanjouw of Utrecht to further this project.

Paleobotany. Seventeen countries were represented on the paleobotanical program. For the first time two sections were organized, one for Paleozoic and the other for Mesozoic and Cenozoic paleobotany. Among the numerous subjects discussed were nomenclature, structure of ancient woods, evolution within various groups, early floras, and classification and affinities of fossil spores and pollen and their use in correlation. Some of the papers dealing with this last topic were given in conjunction with the newly organized section on palynology. More or less neglected subjects were coal ball plants and Tertiary leaf impressions, although some of the broader aspects of Cenozoic floras were treated in several papers. There were a few contributions on paleobotanical techniques. At the special session dealing with nomenclature held before the congress, 31 Dec. 1820 was agreed upon as the starting date for paleobotanical nomenclature. Also a list of generic names passed upon at Stockholm in 1950 was formally placed in the list of *Nomina Conservanda.* The International Committee on Paleobotanical Nomenclature was reorganized. Two steps were taken to increase international cooperation among paleobotanists: one was the setting up of a subsection on paleobotany under the botanical section of the International Union of Biological Sciences, and the other was the creation of a paleobotanical section within the International Society for Plant Taxonomy. Before the congress there was a 3-day excursion into the coalfields of northern France, using Lille as headquarters. Then a 6-day posteongress excursion was made into southern France, where Stephanian and Tertiary fossils were collected. Both trips were directed by Depape and Corsin, professors from Lille.

Ethnobotany. These meetings marked the first time that ethnobotany has been recognized at an international congress of botany by the inclusion of a section under that name. The fledgling section was not large, but it was most energetic and enthusiastic. Active participants were from such countries as France, England, the Netherlands, Yugoslavia, West Germany, Saar, U.S.S.R., Philippines, Belgium, Canada, Iraq, and the United States.

R. Portères and A. Haudricourt (France) deserve considerable credit as organizers of the section, and Jacques Rousseau (Canada) as president of the section carried out this function with his usual vigor and good nature. Baranov (U.S.S.R.) and Jones (U.S.A.), who are vice presidents, took over the chair for a portion of the program. Five independent half-day sessions were held as well as joint sessions with the history of botany section. Papers concerned with a variety of the aspects of the interaction of man and plants were well received, and discussion was quite animated. The subjects covered included edible plants, origin and history of cultivated plants, plant names, plant lore, sacred plants, narcotic plants, and so forth.

The initial session was given entirely to an open discussion of the question "What is ethnobotany?" This session was particularly valuable in that it permitted the presentation of opinions concerning the proper materials and limits for this rather widespread field. There seemed to be general agreement that ethnobotany should encompass all of the various interrelationships between folk cultures and their plant environments. Involved in this interaction are not only the practical economic aspects of plant utilization and technology but also the philosophic aspects of plants in legends, mythology, religion, and in botanical knowledge and concepts of primitive peoples. In addition, it was felt that the effects and influences of man on plants and vegetation should be noted. There was no attempt to arrive at a formal definition of ethnobotany, for it was decided that there is some benefit in a fluidity of the conception of this rather young field.

There was a general feeling that the exchange of data and ideas and the comparison of methods made possible by this section meeting were exceedingly valuable and stimulating to the participants. This was reflected in the unanimous passing of a resolution, favoring the investigation of means for bringing about more effective communication, more frequent colloquiums, and the establishment of ethnobotanical laboratories for the study of materials from various continents.

Ecology and phytosociology. A good deal of attention was given to the question of vegetation mapping on various scales. The precongress colloquium and exhibition were continued, and further contributions were offered by several participants, especially Gaussen and Rey (Toulouse), Emberger and Trochain (Montpellier), Schmid (Zürich), Ozenda (Alger), Hueck (São Paulo), Van Steenis (Leyden), Gams (Innsbrück), and Küchler (Kansas).

Many descriptive inventories of little known areas were also presented. One of the most remarkable was

an evening lecture by Osvald (Uppsala) on the bogs of New Zealand. Lavrenko, Tikhomirov, and Stankof (U.S.S.R.) also presented most interesting materials. The Soviet delegation very generously distributed a number of copies of a handsomely bound and illustrated book containing the Russian and French texts of the papers given by its members. The ecological maps were of special interest.

Papers concerning vegetation dynamics were also quite numerous. The differences in background, training, and philosophy of the proponents led to the usual discrepancies in interpretation. However a good deal of common ground was uncovered.

Taxonomy and chorology. The findings and interpretations of experimental taxonomy were reviewed in a brilliant symposium in which American and British contributions were outstanding. Gilmour (Cambridge) and Heslop-Harrison (London) even proposed a revised nomenclature of the "units of microevolutionary change" that caused a minor tempest and stimulated much useful discussion.

Gams (Innsbrück) gave a spirited criticism of Croizat's recently published theories of plant distribution; Faegri (Oslo) presented a new atlas of the Norwegian flora; Raymond (Montreal) read a new chapter in his phytogeographic studies of *Carex*, which have given us new insights on the migrations of boreal floras; Humbert (Paris) and Cuatrecasas (Chicago) offered new contributions to the *Senecio* and *Espeletia* problems of Madagascar and Colombia.

Protection of nature. Six sessions were devoted to the study of particular areas where nature needs to be protected. Parts of Africa and Madagascar were described and assessed by Troupin (Brussels), Jaeger (Strasbourg), Schnell (Caen), Humbert (Paris), Robyns (Brussels). The main report on the Pacific was given by Fosberg (Washington) who gave special emphasis to a large bog area in Japan that is about to be flooded. Stehlè (Guadeloupe), Hueck (São Paulo), Lasser (Caracas), and Velez (Puerto Rico) reported on tropical America. The presence at most of these meetings of Harroy and Robyns (Brussels), Heim (Paris), Gille (UNESCO), and several others who are connected with the International Union for the Protection of Nature permitted frequent cross-references to the work already done by that organization. The section discussed conservation policies and passed several resolutions in support of national and international organizations that have already made specific recommendations.

In many other sections of the congress important work was done, new facts revealed and new interpretations proposed, that cannot be reported here. A number of activities involving the congress at large took place—among them a visit to Versailles, a reception at the City Hall, excursions to the forest and castle at Fontainebleau, and a visit to the arboretum at Les Barres. Most noteworthy perhaps was a beautiful exhibition of botanical illustrations from the collections of the Museum National d'Histoire Naturelle. The best work of the European illustrators of the 18th and 19th centuries was displayed to great advantage. Another highlight of the congress was the celebration of the 100th anniversary of the Société Botanique de France, whose president, Roger de Vilmorin, made a most elegant speech in four languages. This was followed by a presentation of the botanical landscape of France in a series of colored lantern slides that had been gathered from various collections by Chouard (secretary-general of the congress); they were commented on by him and by several other French botanists, each one covering a different region. On this occasion also, the compliments of some 100 botanical societies from different parts of the world were presented to the Société Botanique de France by foreign delegates. Harriet Creighton (Wellesley College) delivered a most gracious address on behalf of the Botanical Society of America.

The congress was preceded and followed by many excursions of botanical interest. Most of them were concentrated on French territory, but some extended to North Africa and even to other parts of the French Union in tropical Africa. It was my good fortune to join the Ivory Coast expedition, which was led by Mangenot (Paris). This consisted of a month of travel through the tropical rain forest. All arrangements had been made to accommodate 16 people comfortably, to feed them, to give the medical care, and to provide guides and material help, not to mention the scientific information constantly provided by the experienced French botanists. The cost of this trip to the participants was nominal.

The generosity of the French Government and of French scientific institutions is worth putting on record. There is no doubt that the 8th International Botanical Congress was a success, not only because of careful planning and coordination, but also because of strong public support, material and otherwise. Without these special considerations, many foreign delegates could not possibly have afforded the expense, either of attending the congress or of taking part in the excursions. It is to be hoped that such an investment in international exchange will seem worth while to the other countries that will follow France in the organization of botanical congresses. In fact, the next one will take place in Canada in 1959.

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Zoological Nomenclature

On 22 Apr. 1955, the International Commission on Zoological Nomenclature will start to vote on the following cases involving the possible use of the plenary powers for the purpose specified against each entry. Full particulars of these cases were published on 22 Oct. 1954, in pt. 9, vol. 9 of the *Bulletin of Zoological Nomenclature*.

1) Renier [1804] *Prospetto*, question of validation of four generic names (*Discoides*, *Cerebratulus*, *Polycitor*, and *Scolizedon*), published in.

2) Renier [1807] *Tavola*, question of validation of six

generic names (*Aglaja, Alcyonaria, Cystia, Rodens, Tuba,* and *Tubulanus*), published in.

3) Names (generic and specific) given to aptychi of ammonites, suppression of.

4) *Notropis* Rafinesque, 1818 (class Osteichthyes), determination of gender as masculine.

5) *Cheloniceras* Hyatt, 1903 (class Cephalopoda, order Ammonoidea), designation of type species for.

6) *Argus* Bohadsch, 1761 (class Gastropoda), retention of status for purposes of the law of homonymy to preserve *Lysandra* Hemming, 1933, from falling as a synonym of *Argus* Boisduval, 1832.

7) *minimus* Miller (J.S.), 1826 (*Belemnites*) (class Cephalopoda, order Dibranchia), validation of.

A proposal for a "declaration" banning the names based on aptychi of ammonites is also included.

Comments on these cases should be sent as soon as possible to Francis Hemming, Secretary to the Commission, 28, Park Village East, Regent's Park, London, N.W.1.

FRANCIS HEMMING
International Trust for Zoological Nomenclature

Science News

In a statement to the press on 29 Oct., Pierre Auger, French physicist who for 3 yr was the French delegate to the United Nations Atomic Energy Comission and who now heads the natural science section of UNESCO, said that the U.S. plan for **peaceful uses of atomic energy,** first announced by the President last December, requires much clarification and elaboration. He mentioned that a six-paragraph U.S. memorandum, which will be the basis for the next debate on the subject, leaves many major questions unanswered.

The U.S. has called for creation of a new international agency to start work early next year. Auger pointed out that it is not known who will be its members, how the agency will be organized, how it will be financed, or what authorities will run it. The plan calls also for an international scientific parley to be summoned early next year under United Nations auspices. "The conference—like the agency—is not very clear in the minds of many persons," Dr. Auger said.

The following statement was released by the **Atomic Energy Commission** on 26 Oct.:

> The Chairman of the Atomic Energy Commission stated that there had been a series of detonations of nuclear explosives in Soviet territory. This series began in mid-September and has continued at intervals to the present. Further announcement concerning this series will be made if some unusual development would appear to warrant it.
>
> As is generally the case with nuclear detonations, these tests have resulted in some widespread fall-out of radioactive material, but insignificantly in the United States.

Small amounts of **crystalline DL-α-lipoic acid** are available for the use of interested investigators. For details see the communication by L. J. Reed elsewhere in this issue.

A 2-yr research program involving the infection of 154 human volunteers with a **new type of antityphus vaccine** has proved that the vaccine provides a more effective and longer lasting immunity to epidemic typhus than the vaccines in current use. This conclusion was reported at the annual meeting of the American Public Health Association by John P. Fox, professor of epidemiology at Tulane University who was in charge of the research. He stated that the new vaccine resisted the disease 2 yr after initial inoculation, and that a comparison with a commercial antityphus vaccine had demonstrated the superiority of the new material. The agent used by Fox and his associates is strain E of rickettsia Prowazeki, which contains minute doses of living nontoxic typhus germs.

The experimental immunization program was conducted among inmates of Mississippi State Prison. It followed an original project conducted in 1951 among 29 inmates to determine the safety of strain E for human beings. Both projects were preceded by intensive tests on animals by Fox, and limited tests on man by Fox and F. Perez Gallardo of Madrid, Spain, who was the first to isolate this strain of typhus germ.

Fox reported also that 8000 persons in Peru have been inoculated with strain E to determine its effectiveness in a mass immunization. This field test, begun in the summer of 1953 and still continuing, has shown that strain E is effective in producing a good antibody response. It was 92 percent effective in a large group given small amounts of the vaccine and was 97 percent effective in the groups receiving larger amounts. The field research revealed that the most satisfactory method of administering the antityphus agent is in the muscle, and that the dose required is very small.

On 24 Oct. word came from Katmandu, Nepal, that a three-man Austrian expedition had conquered **Mount Cho Oyu,** the world's seventh highest peak. The group consisted of Herbert Tichy, geologist, Josef Joechler, construction engineer, and Helmut Heuberger, geography professor. A report stated that Tichy and Joechler, accompanied by a Sherpa guide named Pasang, reached the crest, where they planted the flags of Austria, Nepal, and India and buried offerings to a goddess supposed to rule the height. The team was said to have made the ascent without the use of oxygen; Cho Oyu is 26,867 ft in altitude. A British expedition, led by Eric Shipton, made an unsuccessful attempt to climb the mountain in 1952.

Two maps, one having the **first known cartographic mention of America** and the other indicating that Portuguese sailors were in the West Indies before Columbus, have been acquired by the University of Minnesota's James Ford Bell Collection. The Waldseemuller globe map, a 9½ by 15 in. wood engraving, was first published in 1507 in St. Die, France, by Martin Waldseemuller, a geographer who was an admirer of Amerigo Vespucci. It was published for use in conjunction with Waldseemuller's book, *Cosmographia Introductio,* that appeared the same year. It was designed to be pasted on a ball and is believed

to be the first published globular map of the Western Hemisphere. The Minnesota copy is thought to be the only one now in existence. Waldseemuller also published a second map, for a flat surface, and on both appeared the name "America."

The second map, a 1424 nautical chart, cartographer unknown, is the first known document in which the name "Antilia" appears. The term is placed near the largest of the Atlantic islands shown on the chart, and Armando Corteseo of Portugal's University of Coimbra declares that the designation of these islands is the first cartographic representation of the "forefront of eastern America." The name "Antilia" is definitely Portuguese in origin and Corteseo has advanced the theory that Portuguese sailors, carried by ocean currents from their home coast, reached the New World before Columbus did.

The **Swedish Geological Survey** has announced that ore bodies with high copper content have been found in the Adak district in the Skellefteå field, North Sweden.

Is **exogamous artificial insemination** a benefit to humanity or should it be considered a crime? Its future hangs on legislation. This important problem is discussed by Wendy Stewart in an article titled "What should the doctor know about exogamous artificial insemination?" appearing in the November *Journal of the American Medical Women's Association*. Some people think artificial insemination so beneficial that it should be encouraged; that the child living in a home where he was so much desired and whose characteristics have been selected, has an unusually good chance of sound development. Others consider the practice a criminal offense, and that the donor must be so depraved that he could contribute only poor hereditary characteristics.

> There are serious aspects of social, moral, and legal welfare to be considered . . . as things stand at present there is much risk of an outcome detrimental to the hoped-for child. At best . . . there is doubt as to his legal status; at worst . . . he is regarded as an illegitimate child.

Instead of forcing legislation prematurely, it would be better, Dr. Stewart feels, eventually to translate existing custom into law. This can come if the practice is demonstrably widespread, with safeguards protecting all concerned. At present most of the problems can now be resolved if the child is adopted legally by the married couple. "While the ultimate goal should be legislation . . . the immediate one should be adoption."

Inspired by the **earthworm breeding farms** he saw in California, as well as by Darwin's estimate that approximately 400 lb of humus a year are ploughed up by the earthworms normally inhabiting an acre of land, a German farmer during the past year has built up a career on these most humble of creatures. He has established Germany's first earthworm farm; he sells a box of 100 worms for DM.1.5 (approximately 36 ct). They are cheaper by the thousand and cheapest of all as spawn. He has not yet, however, reached the production capacity of some California earthworm farms, which are able to send out 500,000 worms a day and which, after the Netherlands flood catastrophe, delivered to that country several million earthworms whose activity contributed towards making the flooded areas arable again.

During a recent interview in New York, Rajkumari Amrit Kaur, Minister of Health for India, reported that in the last 5 yr **life expectancy** in her country has risen from an average of 27 yr to 32 yr. She also referred to progress in the antimalaria campaign as "one of the triumphs of international cooperation."

The 1954–55 **exploration program of the New York Botanical Garden** began with the departure in October of three different parties to northern South America. For the first 3 wk of October John Wurdack, with Nicholas Guppy as his assistant, made a survey of the timber potential of a tract of land in the rainforest south of the Orinoco River in central Venezuela. In December Wurdack will go to the Gran Sabana area of southeastern Venezuela. He will be accompanied by Julian Steyermark of the Chicago Natural History Museum, and together they will explore the tabular sandstone mountains in the Chimanta-tepui region.

Bassett Maguire and Richard S. Cowan went to Amapa, the northeasternmost state of Brazil, in continuance of the Garden's interest in obtaining data on the flora of Venezuela, the Guianas, and adjacent Amazonia. After a week Maguire flew to the upper Branco River in northern Brazil, just south of the British Guiana border, where he is visiting the mountain called Tepequem for several weeks. Cowan will remain in Amapa for a 6- to 8-wk stay before making brief excursions into the forests of French Guiana, Surinam, and British Guiana. These parties are expected to return to New York by the first of March or shortly thereafter.

From the recent annual meeting of the National Association for Mental Health have come these facts about the extent of **mental illness** and the lack of facilities and trained personnel for the care and treatment of the mentally ill. (i) This year about 250,000 persons will be admitted to mental hospitals for the first time. (ii) At the present rate, one of every 12 children born each year will need to go to a mental hospital sometime in his life. (iii) More than one-half of all of our hospital beds are occupied by mental patients. (iv) Mental illness costs us over 1 billion dollars a year in tax funds.

Members of the house of delegates of the Medical Society of Virginia have voted to **admit Negro doctors** to membership in their State medical society. The District Medical Society (D.C.) and the Maryland State Medical Society have taken similar action in past years.

Scientists in the News

Linus Pauling, winner of the 1954 Nobel Prize in chemistry [*Science* **120**, 796 (12 Nov.)] has made many contributions to science, but his most important was his discovery of the fundamental principles determining the nature of the chemical bond and the structure of molecules. This has led him to his discoveries concerning the essential atomic structure of proteins, including such physiologically important materials as hemoglobin, blood serum, enzymes, hair, skin, and muscle.

Pauling and his associates began working on the molecular structure of proteins, the major component of all living cells, in the mid-thirties. Proteins are so complicated that their structure could not until recent years be determined. Unlike most other chemicals, which consist of only a score or two of individual atoms, protein molecules are made up of thousands, even millions, of atoms; therefore instead of trying to study protein molecules directly, Pauling first investigated their component parts, such as the amino acids. Analyzing these by x-ray diffraction, he ultimately obtained enough information to permit a precise prediction of the configuration of the oxygen-hydrogen-nitrogen-carbon chains that form the backbone of protein molecules.

It is hoped that knowledge of the atomic structure of proteins will be a valuable tool in medical research. Pauling and his colleagues have already found that sickle-cell anemia is associated with an abnormality in hemoglobin molecules. During the past 2 yr Pauling has been working on the structure of collagen, the protein that occurs in tendons, bones, and skin. It is probably the most important protein in the human body, for it gives strength and toughness to tissues. There is evidence now that many diseases, such as arthritis, seem to involve some abnormality in the manufacture or structure of this protein.

For many years Pauling has also been interested in the structure of metals and alloys and the relation of structure to properties of these substances. Between 1938 and the present he has been working on the development of a theory of the electronic structure of metals and alloys that differs considerably from the quantum mechanics theory that is generally accepted. A principal difference is that Pauling assumes that a larger number of electrons are involved in bonding the atoms together than has previously been thought. Some 2 yr ago he applied his general ideas about metals in the statement of a new theory of the ferromagnetism of iron and other magnetic substances.

Recently Pauling, Robert B. Corey, and Richard E. Marsh have completed a detailed investigation of the molecular structure of silk. Silk fibers are very strong —stronger than the strongest steel wires with the same cross-sectional area—and Pauling and his associates explain this strength; the structure of silk involves extremely long molecules of silk protein, extending in the direction of the fibers. These molecules are attached to one another by hydrogen bonds, which connect each molecule with two others, one on each side. These molecules form what the investigators term "pleated sheets" and silk fiber consists of many of these sheets arranged side by side. The great strength of the fiber results from the fact that, in order to break it, it is necessary to break the molecules themselves—that is, to break chemical bonds between atoms of carbon and nitrogen.

Pauling's experimental research includes the determination, by x-ray diffraction, of the structure of about 50 crystals, and, by electron diffraction, of about 60 gas molecules. In the general field of molecular structure, his discoveries of fundamental principles include: the hybridization of bond orbitals and the theory of directed valence (1928); the relation of hybrid bond orbitals to magnetic properties of substances (1931); the partial ionic character of single bonds and its relation to heats of formation of substances (1932); the resonance of molecules among two or more electronic structures and the determination of the configuration of molecules through resonance, such as the planarity of conjugated systems (1932); and the correlation of interatomic distances and other structural features with electronic structure (1932). In the elucidation of protein structure, Pauling's contributions include the discovery of the extraordinary magnetic properties of hemoglobin and their interpretation in terms of molecular structure (1936, with C. D. Coryell); the development of a general structural theory of native, denatured, and coagulated proteins (1936, with A. E. Mirsky); the formulation of a theory of molecular structure of antibodies and the nature of serologic reactions (1940); the discovery that an abnormality in molecular structure of hemoglobin is responsible for sickle-cell anemia (1949, with H. A. Itano, S. J. Singer, and I. C. Wells); and the discovery of the configuration of polypeptide chains in some fibrous and globular proteins (1950, with R. B. Corey).

Benjamin Miller, senior associate physician at Peter Bent Brigham Hospital, Boston, and lecturer on medicine at Harvard Medical School, has been appointed director of the Jewish Hospital Association's May Institute for Medical Research in Cincinnati. He has conducted research for 20 yr in the field of kidney diseases and allied conditions such as high blood pressure. He plans to continue studies on kidney transplantation and in the broad field of kidney diseases and related conditions of cardiovascular diseases. He will also participate in the teaching program of the association.

Two members of the Soviet Academy of Sciences, **Andrei Levovich Kursanov,** a physiologist, and **Boris A. Rybakov,** a professor of social sciences, attended the closing ceremonies of Columbia University's bicentennial. The Russian scientists' visit to the United States, the first of its kind in several years, resulted from the Soviet Academy's acceptance, only a few days before the event, of an invitation sent more than 4 yr ago.

The Upjohn Co. has announced the transfer of **Harold R. Reames** from the medical division to the research division where he will head the department of infectious disease. Reames has been with the company since 1951 in the department of clinical investigation of new drugs.

Louisiana State University School of Medicine has established a new annual lectureship in honor of **Peter Graffagnino** of New Orleans, the first professor in the university's department of obstetrics and gynecology. The initial Graffagnino lecture was given on 27 Oct. by **Edward A. Schumann,** professor of obstetrics and gynecology at the University of Pennsylvania Medical School.

Lord Rothschild, director of research in the department of zoology at Cambridge University, England, is visiting the California Institute of Technology to continue his research in the field of embryology. Appointed research associate in biology, he is working with Albert Tyler on some problems of the early phases of both plant and animal reproduction.

The Institute of Radio Engineers has named **Harald T. Friis,** director of radio research at Bell Telephone Laboratories, Red Bank, N.J., the recipient of the IRE medal of honor, the highest technical award in the radio engineering profession. The award, which was given "for his outstanding technical contributions in the expansion of the useful spectrum of radio frequencies, and for the inspiration and leadership he has given to young engineers," will be presented during the IRE national convention in New York next March.

The Morris Liebmann memorial prize, awarded annually to an IRE member who has made a recent important contribution to radio engineering, was given to **Arthur V. Loughren,** director of research at the Hazeltine Corp., "for his leadership and technical contributions in the formulation of the signal specification for compatible color television."

Bernard Salzberg of the Naval Research Laboratory, Washington, D.C., received the Harry Diamond memorial award, which is given to persons in government service for outstanding work in radio and electronics. The award was presented "for his contributions in the fields of electron tubes, circuits, and military electronics."

The Vladimir K. Zworykin television prize award went to **Harold B. Law,** RCA Laboratories Division, Princeton, N.J., for his contributions to the development of the shadow-mask tricolor television picture tube.

Milton Helpern, chief medical examiner of the City of New York, has been appointed professor and chairman of the department of forensic medicine in the New York University–Bellevue Medical Center Post-Graduate Medical School. Halpern joined the faculty of the N.Y.U. College of Medicine in 1934 as a lecturer in forensic medicine and became an associate professor in the Post-Graduate Medical School of the Medical Center in 1949. He is also assistant professor of clinical medicine and lecturer in pathology and legal medicine at Cornell University Medical College, lecturer in criminologic medicine at the New York Police Academy, and honorary lecturer in forensic medicine at the University of Southern California Medical School.

The annual John McReynolds lecture in ophthalmology for 1954 was given at the University of Texas Medical Branch, Galveston, on 15 Oct. by **A. Francescotti,** director of the ophthalmology clinic of the University of Geneva in Switzerland. He spoke on "Cataract in relation to hereditary skin disorders." The lectureship was established in honor of the late J. O. McReynolds of Dallas, pioneer ophthalmologist of the Southwest.

Other recent distinguished visitors at the Galveston Medical Branch have been **Francis E. Camps,** professor of forensic medicine at the University of London, and **Neville F. Stanley,** director of epidemiology in the Public Health Service of New South Wales, Australia.

William B. House, formerly associated with the National Alfalfa Dehydrating and Milling Co. of Lamar, Colo., has been appointed a research chemist at the Midwest Research Institute, Kansas City.

H. J. Beattie, Jr., and **F. L. VerSnyder** of the General Electric Co., West Lynn, Mass., have been jointly awarded the 1954 Henry Marion Howe medal for their paper "Microconstituents in high temperature alloys," published in the *Transactions* of the American Society for Metals.

Among the Independence Day decorations that were awarded by the President of India, the following honors were given to scientists and educationalists. The Bharat Ratna was received by the Vice President, philosopher and educationalist Servepalli Radhakrishnan, and by the physicist **C. V. Raman.** The Padma Vibhushan Pahala Varg (1st class) was awarded to physicist **Satyendranath Bose,** and educationalist **Zakir Husain.** The Padma Vibhushan Dusra Varg (2nd class) was awarded to 19 people, including scientists **H. J. Bhabha, S. S. Bhatnagar,** and **K. S. Krishnan.**

Callaway Brown, senior chemist at Armour Research Foundation of Illinois Institute of Technology, Chicago, has been presented the award of scientific merit by the foundation's chemistry and chemical engineering research department for research on the manometric determination of the density of liquid ozone. The work was sponsored by the Government.

Joel Warren, formerly chief of the department of bacteriology, Army Medical Service Graduate School, Washington, D.C., is now serving as science attaché for Scandinavia and is stationed at the American Embassy in Stockholm, Sweden.

Yehia Aziz Habib, who is on leave of absence from the faculty of medicine of the University of Alexandria, Egypt, has been appointed visiting associate professor of clinical physiology at the University of Tennessee College of Medicine. His research work has been primarily in the kidney physiology of mammals.

Paul A. Miller, professor of sociology at Michigan State College since 1947, has been named deputy director of the Michigan Cooperative Extension Service.

Two engineering appointments at AC Spark Plug Division of General Motors have been announced. **Karl Schwartzwalder,** chief ceramic engineer, has been named director of research, and **Wilfred A. Bychinsky,** chief ignition engineer, has been promoted to assistant chief engineer in charge of spark plug work. Formerly spark plug engineering and research were under the direction of Taine G. McDougal, who retired recently.

Wendell M. Latimer, University of California chemistry professor who has made important contributions to national defense in the fields of atomic energy and chemical warfare, has been awarded the 1955 William H. Nichols medal of the American Chemical Society's New York Section. A pioneer in low temperature research in the United States, Latimer was active during World War II in National Defense Research Committee studies of oxygen production, toxic gases, and plutonium. From 1943 to 1947 he was director of a Manhattan Engineering District project on the chemistry of plutonium, which was carried out by the University of California Department of Chemistry. Since then he has been associate director of the university's Radiation Laboratory. He also supervised wartime research on the effect of weather conditions upon the behavior of toxic gases.

James Hillier, who has been director of the research department of Melpar, Inc., a subsidiary of the Westinghouse Air Brake Co., has joined the research and engineering staff of the Radio Corporation of America as an administrative engineer. Hillier was associated with RCA Laboratories from 1940 to 1953, first as a research physicist and later as supervisor of fundamental electron microscope research.

The following appointments to assistant professor have been announced. Philadelphia College of Pharmacy and Science: **Robert E. Abrams,** pharmacy. Florida State University: **Conway W. Snyder,** physics. Tulane University: **Leo F. Kock,** botany.

Henry A. Imus, formerly head of the physiological psychology branch at the Office of Naval Research, has been appointed assistant to the director of the National Institute of Neurological Diseases and Blindness of the National Institutes of Health. His new duties involve program analyses and program development in the fields of neurological diseases and sensory disorders.

In the department of chemistry at the University of Southern California, **Robert D. Vold** has returned from his sabbatical year in the Netherlands to resume his duties as professor of colloid chemistry, and **Arthur W. Adamson** and **Karol J. Mysels** are on sabbatical leave this fall. Adamson left on 27 Oct. for Copenhagen where he will work in Bjerrum's laboratory.

Harriet C. Jameson has been appointed chief of the history of medicine division of the Armed Forces Medical Library, Washington, D.C. She joined the division as head of the catalog section in 1950.

Christina C. Hilbrandt of the index-catalogue division retired on 30 Sept. after more than 36 yr of continuous employment in the preparation of the *Index-Catalogue*. In recognition of long and faithful devotion to duty, a certificate of merit signed by the Surgeon General of the Army and the director of the Armed Forces Medical Library was presented to Miss Hilbrandt. She established a record of 26 yr of continuous service without the loss of a day charged to sick leave.

Necrology

Carl E. Arvidson, 56, electrical engineer and vice president of the Consumers Power Co., Jackson, Mich., 20 Oct.; **Robert A. Budington,** 82, professor emeritus of zoology at Oberlin College, Oberlin, Ohio, 23 Oct.; **Austin H. Clark,** 73, investigator in oceanography, ornithology, entomology, and marine biology, authority on butterflies, author, and retired curator of echinoderms at the Smithsonian Institution, Washington, D.C., 28 Oct.; **Bernard A. Etcheverry,** 73, author and professor emeritus of irrigation engineering at the University of California, Berkeley, Calif., 26 Oct.; **James T. Jardine,** 72, agricultural scientist, investigator in the use of forest land for grazing, former director of the Oregon Agricultural Experiment Station, and retired director of research for the Dept. of Agriculture, Washington, D.C., 24 Oct.; **Thomas F. Larkin, Jr.,** 42, civil engineer with the Consolidated Edison Co., New York, 21 Oct.

Paul E. Miller, 65, agronomist and former director of the University of Minnesota Agricultural Extension Service, Minneapolis, Minn., 21 Oct.; **Bryan Hugh O'Neil,** 49, archeologist and inspector of ancient monuments, London, 24 Oct.; **Harry Spaulding,** 69, authority in the field of traumatic surgery and first president of the American Academy of Compensation Medicine, New York, 20 Oct.; **Swain J. Swainson,** 53, former supervisor of operations at the Atomic Energy Commission's research laboratories in Winchester, Mass., and head of the mineral processing laboratories of the American Cyanamid Co., Stamford, Conn., 22 Oct.; **Francis Witmer, Sr.,** 81, former head of the civil engineering department at the University of Pennsylvania, Philadelphia, Pa., 27 Oct.

Meetings

The relationships among living units, from cells to human beings, were deliberated in a 5-day **Josiah Macy, Jr., Foundation Conference on Group Process** that took place 26–30 Sept. at Cornell University. This was the first of five annual conferences on the general subject of "group process." The participating scientists from this country and abroad represented anthropology, biology, ethology, medicine, psychology, psychiatry, and zoology. The conference began with an open house at the Cornell University Behavior Farm Laboratory. Howard S. Liddell, A. U. Moore, and Helen Blauvelt of Cornell gave demonstrations of conditioning under stress in goats.

The conference's purpose was stated by Frank Fremont-Smith, medical director of the Macy Foundation, who also explained that the conference was devoted to informal discussions and free interchange of data, ideas, and concepts rather than to formal presentations. Liddell, director of the Cornell Laboratory, was conference chairman. Among the nine "members" who attended all five conferences, were Margaret Mead of the American Museum of Natural History in New York and Erik Erikson of the Astin Riggs Foundation in Stockbridge, Mass., anthropologists; Jerome Bruner of Harvard University, Harris B. Peck of New York, and Liddell, psychologists; Frieda Fromm-Reichmann of the Chestnut Hill Sanitorium in Rockville, Md., and John Spiegel of the Psychological Clinic in Cambridge, Mass., psychiatrists; Jerome Frank of the Johns Hopkins University School of Medicine, group psychotherapist; and Eckhardt Hess of the University of Chicago, ethnologist.

Four day-long discussion sessions were held: "General principles of development," led by Frank A. Beach of Yale University; "Psychology and ethology as supplementary parts of a science of behavior," Niko Tinbergen of Oxford University; "Dynamics of the mother-newborn relationship in goats," H. Blauvelt of Cornell; and "Innate motor and receptor patterns," Konrad Z. Lorenz of the Max Planck Institute for Ethology in Germany.

On 6–9 Dec. the **Entomological Society of America** will hold its second annual meeting since the reorganization of 1 Jan. 1953. About 600 to 800 members and guests are expected to gather for the program that includes more than 160 scientific papers arranged under the supervision of W. R. Horsfall of the University of Illinois, program chairman. Meeting headquarters will be in the Rice Hotel, Houston, Tex.

The general sessions of the meeting will be presided over by H. H. Ross of the Illinois Natural History Survey, president of the E.S.A. A special feature will be recognition of the centennial of professional entomology by two invited speakers: Roger C. Smith (Manhattan, Kan.) will speak on "Entomology and its accomplishments," and P. J. Chapman (Geneva, N.Y.) has "Entomology and its future" as his topic. Among the other invited addresses to be given are "Arthropod transmitted virus diseases in Trinidad, B.W.I., with special reference to yellow fever" by Dr. Wilbur D. Downs, Rockefeller Foundation; "The interrelations of biological control and taxonomy" by Curtis W. Sabrosky, U.S. Department of Agriculture; "The ecological approach to management of insect populations" by J. H. Pepper, Montana State College.

Partially because of the meeting's proximity to Kerrville, Tex., where the U.S. Department of Agriculture conducts important research on insects attacking domestic animals, the sessions devoted to medical and veterinary entomology will be particularly active. An innovation at the meeting will be the conduct of three concurrent sessions on the morning of 8 Dec. that are so closely scheduled that the exact time of each speaker's presentation will be known to all.

The **AAAS Committee on Social Physics** has organized two sessions in Section K—Social and Economic Sciences that are to take place on 27 Dec. during the association's annual meetings in Berkeley, Calif. This program is under the chairmanship of S. C. Dodd of the Public Opinion Laboratory, University of Washington, Seattle, and is built around the topic *Diffusion Theory—Contributions Towards Interdisciplinary Unifying of Mathematical and Semantic, Physical and Biological, Psychological and Sociological Models and Experiments*. Papers formally synthesizing diverse points of view are being prepared, exchanged, and revised in view of the other papers. Contributors are Anatol Rapoport, Nicholas Rashevsky, H. D. Landahl, Henry Winthrop, Richard J. Hill, Stuart C. Dodd.

Available Fellowships and Awards

Under a program devised jointly by **McGill University** and the **Arctic Institute of North America** and supported financially by the **Carnegie Corp.** of New York, certain scholarships are offered to students possessing a bachelor's or master's degree or the equivalent. These scholarships are tenable at McGill University, Montreal, and are normally offered to students proceeding to a doctoral degree in a subject calling for active field research in arctic or subarctic North America. Candidates who do not intend to proceed to a degree are not necessarily disqualified.

Such subjects as anthropology, bacteriology, botany, geography (including glaciology and meteorology), geology, genetics, parasitology, psychiatry, psychology, sociology and zoology will be considered, and successful candidates will be enrolled in one of these departments. In arriving at decisions the committee will bear in mind the general furtherance of northern research and also the physical as well as academic suitability of candidates.

The scholarships are normally for 1 yr and average $1250 for the academic session and $1000 for the expenses of a summer's field expedition. Applications should be submitted to the secretary of the Carnegie Arctic Program, Arctic Institute of North America,

3485 University St., Montreal, P.Q., and should include a confidential recommendation of the candidate's qualification in his or her selected field and a clear statement of the intended arctic or subarctic research project. *Applications for the 1955–56 session should reach Montreal by 1 Apr. 1955.* If field work in the summer of 1955 is anticipated, applications must be in *by 1 Jan. 1955.*

Under another McGill–Arctic Institute–Carnegie program an annual fellowship is offered. This $4000 fellowship, tenable at McGill, is for a senior candidate who has engaged in suitable arctic or subarctic field projects and who requires a year's residence at a center that specializes in arctic learning in order to prepare a monograph or a book or to continue study in a field connected with arctic or subarctic problems. It is intended primarily for senior candidates who have already completed their academic training. Applications for this fellowship should also be submitted to the secretary of the Carnegie Arctic Program. *The deadline for 1955–56 is 1 Jan. 1955.*

The American Academy of Arts and Sciences is offering the **Francis Amory septennial prize** for outstanding work addressed to the alleviation or cure of diseases affecting the human reproductive organs, in particular those of men. No formal applications and no essays or treatises from candidates are desired; but nominations, supported by statements of qualifications in respect to work consummated between 10 Nov. 1947 and 10 Nov. 1954, will be *accepted until 1 Dec.* These should be sent to 28 Newbury St., Boston 16, Mass.

The **Atomic Energy Commission** has recently established a marine biological laboratory at Eniwetok in the Marshall Islands. The laboratory has a twofold purpose: to serve the AEC in connection with biological studies related to atomic test activities; and to make facilities available to university biologists who are interested in conducting fundamental studies. The location of the laboratory provides unusual conditions for biological studies of marine and land animals and plants of the Central Pacific area.

Eniwetok Atoll lies 2500 mi southeast of Hawaii and is made up of a circle of small coral islands approximately 20 mi in diameter. Most of the islands are covered with tropical vegetation, but a few have been extensively cleared to facilitate operations during test periods. Islands and coral reefs suitable for field studies can be reached by boat and aircraft.

The laboratory, which will accommodate up to 10 investigators at a time depending upon operational requirements, is well equipped for biochemical and general laboratory procedures. Facilities for maintaining organisms in running sea water are provided. Collecting gear is available for offshore studies.

For projects that will be beneficial to the national welfare or the scientific interests of the United States, the AEC will consider limited sponsorship of investigations. That is, for investigators with approved projects, the AEC will provide laboratory space, the usual laboratory supplies, and transportation to the laboratory. Lodging and food are available at a nominal cost. Inasmuch as Eniwetok is a restricted area, AEC security clearance is required of all investigators. Inquiries should be directed to the Biology Branch, Division of Biology and Medicine, Atomic Energy Commission, Washington 25, D.C.

In the Laboratories

The Ercona Corp., New York, exclusive American agent for VEB Carl Zeiss Jena, instrument manufacturing firm in the Eastern Zone of Germany, has included the following statements in a recent letter to the editors about **Zeiss in Germany.**

> We were quite disturbed to note . . . the report [*Science* **120**, 23 (2 July 1954)] concerning the status of Zeiss in Germany, as submitted by Carl Zeiss, Inc., New York, the *former* exclusive representatives of the great optical firm of Carl Zeiss Jena. . . . The injustice suffered by the VEB Carl Zeiss Jena and the Ercona Corporation . . . and our desire to clarify the controversy occasion this letter.
>
> By virtue of its unique organization and of its former plants in Jena operating under its charter, the Carl Zeiss Foundation in Jena acquired a worldwide reputation for opto-fine mechanical productions of superb quality. On the strength of the spirit and letter of the original charter of Professor Dr. Ernst Abbe, its founder, the city of Jena has been specifically and for all times stipulated as the domicile of the Carl-Zeiss-Stiftung. . . .
>
> Following World War II, the Carl-Zeiss-Stiftung Jena organized in Western Germany the firm Zeiss-Opton, G.m.b.H., with Heidenheim as the domicile. The former executives of Carl Zeiss Jena resigned their posts and functions in 1945 and submitted to the administration of the Carl-Zeiss-Stiftung proposals for the appointment of new executives, which were then accordingly appointed. One of these executives was Dr. H. Schrade, who is now directing the affairs of VEB Carl Zeiss Jena. The new executives then entrusted the resigned executives with the administration of the Zeiss-Opton, G.m.b.H., then established in Western Germany.
>
> Some time after 1949, the former executives, who had resigned their posts in 1945, tried to obtain hold of the entire administration of the foundation although having . . . expressly declared in their letter of January 28th, 1946, that they no longer held any functions in the Carl Zeiss Foundation in Jena. Despite the plainly formulated clauses of the charter, the former executives created a firm by the name of "Carl Zeiss, Oberkochen" which, incidentally, has nothing whatsoever to do with the Jena works. The Oberkochen firm is not legally entitled to the use of the name "Zeiss." The Carl Zeiss Foundation, Jena, has started procedings before the Provincial Court of Stuttgart opposing the adoption of the aforesaid title.
>
> What cannot be resolved, however, in any court is the undisputed fact that the Zeiss works continue to operate in Jena as a national corporation which employs today well over 18,000 skilled workers. . . . It has been our happy privilege to provide for the last five years many . . . instruments to satisfy the demands of science and industry. The acceptance

thereof on the part of a demanding clientele is sufficient . . . proof of the quality inherent in those products.

The subsequently organized firm of "Zeiss-Opton, G.m.b.H.," which, we repeat, forms part of the Carl-Zeiss-Stiftung Jena and employs about 2800 workers, has been incorporated in the firm Carl Zeiss Heidenheim by the manipulations of a small group of persons in Western Germany. It is the adoption of the name "Zeiss" which is now being vigorously opposed by the Carl Zeiss Foundation, Jena, before the Stuttgart court.

The products of VEB Carl Zeiss Jena are now as before available. . . . .

Plans have been completed for the construction by **American Potash and Chemical Corp.** of a plant for the manufacture of lithium chemicals near San Antonio, Tex. This facility will be owned by a newly formed company, **American Lithium Chemicals, Inc.**, 50.1 percent of whose stock is held by American Potash and the balance by Bikita Minerals (Private) Ltd. Lithium ores for the plant will be supplied by the latter company from its large deposit of lithium ores in Southern Rhodesia. Initial production at San Antonio will be lithium hydroxide.

A major construction program involving the expansion of the **Atomic Energy Commission's** feed materials production and processing plants at three sites has been announced. The total cost of the program is estimated at approximately $67,000,000. It involves construction of a new facility in the St. Louis, Mo., area and expansion of existing facilities at the Feed Materials Production Center at Fernald, Ohio, the feed materials facilities at St. Louis, and the feed plant at the gaseous diffusion plant at Paducah, Ky. The three installations are operated for the AEC by, respectively, the Mallinckrodt Chemical Works, The National Lead Co. of Ohio, and the Union Carbide and Carbon Corp.

The function of the St. Louis and Fernald feed materials plants is to convert high-grade uranium ore and concentrates into highly purified uranium compounds or metal. The Paducah facilities will contribute to the commission's capacity to convert uranium into forms useful to its program. The expansion will substantially increase the nation's production of materials for use in atomic energy programs.

Miscellaneous

The U.S. Fish and Wildlife Service hopes that hunters will return metal **leg bands recovered from wild game** or other migratory birds, along with information about where and when the birds were shot. It has been estimated that 500,000 birds are banded each year and that a total of 7 million birds have been tagged to date.

The bands often reveal much about the bird's traveling habits. A young pintail, for example, was banded in Labrador on 7 Sept. 1951, and was caught in England 2 wk later on 25 Sept. 1951. Other pintails have illustrated this bird's amazing range of travel. A pintail banded in Alaska in the summer of 1950 was caught in Delaware in the fall in 1951. Still other pintails have been banded in North Dakota and recovered in Colombia, South America; banded in California and found in New Zealand; and banded in Hawaii and caught in Alberta, Canada.

This method of keeping a record of migratory birds also gives the researcher some indication of the bird's age. For instance, a mallard banded in California in 1932 was recovered 20 yr later. The oldest record of longevity, however, was a Caspian tern that was banded in Michigan in the summer of 1925 and taken as a scientific specimen in Ohio in 1951, 26 yr later.

Each person who returns a band to the U.S. Fish and Wildlife Service, Washington 25, D.C., receives a letter telling of the bird's banding and any additional biography that may have been collected from other leg band reports.

The Department of Commerce and the Small Business Administration have jointly issued a paper-bound book entitled ***Chemical Products and Processes.*** It contains 1350 abstracts or brief descriptions of Government-owned inventions in the chemical field. The purpose of the book is to let the public, and particularly the small business man, know what Government-owned chemical inventions can be exploited. The inventions are ordinarily available on royalty-free license. The new book can be obtained for $3 from the Office of Technical Services, U.S. Dept. of Commerce, Washington 25, D.C. Similar books on patents in other industries are also available.

Appearing in the December issue of ***The Scientific Monthly*** are five papers on *Perspective and Horizons in Microbiology,* by L. W. Jones, S. A. Waksman, A. J. Kluyver, J. Trefouel, and H. Von Euler-Chelpin, these being based on papers presented at the recent dedication of the Institute of Microbiology, Rutgers University. Other featured articles are "Storm of Balaklava and the daily weather forecast" by H. Landsberg; "Photosynthetic reclamation of organic wastes" by H. B. Gotaas, W. J. Oswald, and H. F. Ludwig; "Role of aircraft in forest-pest control" by E. W. Johnson; "The preacher talks to the man of science" by H. R. Rasmusson; "Ehrlich, biologist of deep and inspired vision" by Iago Galdston. Other contents of the issue include "Science on the march," four letters to the editors, and 25 book reviews.

Research **laboratories serving industry** are being listed anew by the National Academy of Sciences and the National Research Council, Washington. Officials of these organizations are on the search for new laboratories or others that might have been overlooked in previous directories.

The ***Gulf of Mexico—Its Origin, Waters, and Marine Life,*** designated as Fishery Bulletin 89, may be purchased for $3.25 per copy from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

Book Reviews

Vegetable Fats and Oils. E. W. Eckey. ACS Monograph Series. Reinhold, New York, 1954. ix + 836 pp. Illus. $16.50.

More than 10 years have passed since the publication of the second edition of *Vegetable Fats and Oils* by G. S. Jamieson, a most extensive and authoritative survey of the sources, preparation, composition, characteristics, and practical applications of the various fatty products obtained from plants. In the present volume, the title, aims, and scope of Jamieson's book, now out of print, have been retained, and the information has been considerably enriched and thoroughly brought up to date. However, Eckey's book cannot be regarded merely as a new and revised edition of the earlier volume. The introduction and the first seven chapters supply the basic information concerning fats in general, including their composition, physical and chemical characteristics, metabolism in animals, biological synthesis in plants, and methods of analysis. I was especially impressed with the excellent treatment of the physical properties of fats. Of course, in order to keep the size of the book within reasonable limits, much information had to be omitted or mentioned only in a cursory manner. This seems especially regrettable for the short chapter on "Methods" in which only the general principles of the various tests are outlined. In Jamieson's book this section occupied as much as one-fifth of the total number of pages; and for each determination or test, at least one standard procedure was described in such detail that the reader could have used the procedure directly without referring to specialized manuals.

As in the earlier volume, the largest portion of Eckey's book is devoted to the systematic description of nearly all the vegetable fats and oils for which analytic data are available. The older grouping into drying, semidrying, and nondrying oils has been abandoned, and the material has been arranged solely on the basis of the botanical classification of the plants from which the oils are obtained. Furthermore, for each plant, the information concerning the physical characteristics, the chemical composition, and the technologic applications of the oil is preceded by a concise description of the plant itself and of the nonfatty products that may be prepared from the various parts of the plant, including the fat-bearing part. Thus, not only in the general arrangement of the book, but also in the treatment of the individual topics, the emphasis has been shifted from the purely analytic and technologic data on the oil to the relationships between these data and the biological characteristics of the plant producing the oil. These relationships are further underlined in the numerous tables, in which the values for the various oils obtained from plants of the same genus or family are compared. In this respect one might well quote the statements made years ago by T. P. Hilditch that "the fatty (glyceride) components of seeds are specific and closely related to the families in which the parent plants have been grouped by botanists," and that, even in cases in which a peculiar fatty acid, such as erucic, petroselinic, or ricinoleic acid, is present as a major component of the seed oil, "the occurrence of these unusual features runs remarkably parallel with the groups in which morphologists have placed the plants."

Such an approach, together with the clear and fluent style, makes Eckey's book very pleasant and thought-provoking reading. Moreover, because of its complete and up-to-date information, this volume will continue to be what its predecessor has been for many years: a veritable encyclopedia on the subject and an invaluable reference book for all research and technical workers who are interested in the chemical, biological, and practical aspects of vegetable fats.

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Metabolism of Steroid Hormones. Ralph I. Dorfman and Frank Ungar. Burgess, Minneapolis, Minn., 1953. vi + 170 pp. Illus. $4.

During the last 15 years knowledge of the metabolism of the steroid hormones has increased rapidly, largely because of the development of relatively specific microtechniques for these compounds. This book is written by two major contributors to the field. It gives in outline and tabular form their accumulated information on the subject; textual material is limited to that necessary to give meaning to the charts and tables that are used for the major presentation. The book is prepared so that a person having only a limited familiarity with steroids can understand the structures and processes discussed. The term *steroid hormone,* however, is not defined, and therefore the distinction between biosynthesis of the hormones and their further metabolism is not always easy to discern.

The introduction outlines in simple terms some of the techniques that have been useful and gives the structural basis for steroid nomenclature. It is followed by a chapter on steroids isolated from natural sources, the conjugated forms in which they occur, and (a very important point) artifacts produced during the hydrolytic procedures often used in isolation. The next chapter deals with biosynthetic reactions in mammalian tissues as demonstrated by over-all studies using isotopes, by perfusion of specific tissues, or by incubation of tissue slices or homogenates. A separate chapter is devoted to microbiological reactions.

The fifth chapter, according to its title, deals with the "Reactions of steroid hormones in mammals." The title should more appropriately be that used on the tables in the chapter: "Reactions involving steroid

hormones and related substances," since not all of the substrates listed have been demonstrated to be steroid hormones or substances that would be formed from them. The chapter is divided into four sections. Two deal with the reactions of the neutral and phenolic steroids observed *in vivo* and two with the *in vitro* reactions. The former are reactions that would be necessary to explain the formation of a compound isolated from the urine after the administration of a given steroid substrate. The *in vitro* reactions are those that would be necessary to account for the formation of an identified product or structure after incubations with tissues. There is considerable repetition of information given in previous chapters, since all reactions of the neutral or phenolic steroids having 21 carbons or less are tabulated, but the emphasis here is on type of chemical transformation rather than on its role in the organism. The next chapter, "Enzymes influencing steroids," again involves repetition of much material covered under biosynthesis and *in vitro* reactions. In this chapter, however, the types of tissue preparation and the cofactors used are listed.

The next two chapters are given over to an ingenious organization of the previously covered material on the basis of chemical structure. The seventh chapter, "A complete system of steroid metabolism," is largely made up of a series of charts in which certain compounds are taken as key structures, and the various reactions that have been postulated in the previous chapters are organized around them. In the eighth chapter the authors attempt to deduce the effect of structure on the subsequent metabolic reactions and to outline the metabolism of certain steroids on the basis of the reactions and urinary products already discussed. Here an oversimplification enters, for it is implied that all the urinary steroids are formed by enzymes in the tissues of the mammal (usually human) from which the urine has been obtained. This ignores the possible role of the intestinal environment during biliary-enteric recirculation of steroid metabolites, apparently a rather general phenomenon. The last chapter deals with rather general considerations, such as the importance of method, the probability of conversion of C_{19} steroids to C_{21} compounds, and a discussion of the apparent differences between the results of *in vivo* and *in vitro* studies.

For the experienced worker, this book can be very useful as a quick reference for information that would otherwise require hours of library work. Also, in some of the tables space has been provided for the addition of further data as they appear. Thus the usefulness of the outline as a reference can be maintained. The organization of the material according to certain concepts also offers a challenge to test the hypotheses as well as a basis for associative memory. There is danger, however, that the scientist who uses this book to bring himself abreast of an unfamiliar field will be led to false conclusions. For, in the later chapters, chemical organization is achieved at the expense of lack of distinction between biosynthetic processes in the endocrine tissues and the further metabolism of the hormones. Further, as already noted, at no place in the book is the possible role of intestinal environment during hepatoenteric recirculation mentioned. Thus an unwarranted impression of certainty may be obtained regarding certain processes that are, at present, hypothetical. If these factors are kept in mind, however, the book can be a very valuable reference work and a guide to investigations that will determine the significance of the reactions indicated.

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Representative Chordates. A manual of comparative anatomy. Charles K. Weichert. McGraw-Hill, New York–London, 1954. vii + 204 pp. Illus. $3.50.

This laboratory guide for the dissection of four representative vertebrates (the marine lamprey, *Petromyzon marinus*; the spiny dogfish, *Squalus acanthias*; the mud puppy, *Necturus maculosus*; and the cat, *Felis domestica*) is designed as a companion volume to the author's *Elements of Chordate Anatomy*. It contains 103 illustrations.

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Qualitative Analysis and Chemical Equilibrium. T. R. Hogness and Warren C. Johnson. Holt, New York, ed. 4, 1954. xiii + 621 pp. Illus. $5.

In this revision the authors have reached effectively their announced objectives of presenting a considerable body of related theory and a workable short laboratory course in qualitative analysis that is adaptable both to semimicro and macro work. The procedures are, however, given in terms of semimicro operation using the centrifuge.

The theoretical section occupies slightly more than one-half of the volume. A considerable amount of pertinent descriptive chemistry and facts about equilibria precedes each laboratory procedure for a group of elements. The inclusion of a chapter on quantized atoms and molecules and another chapter on nuclear chemistry may represent unnecessary material in many institutions. The other 12 chapters of the theoretical material are standard material for many courses that cover general chemistry and qualitative analysis. The discussion of complex-ion formation has been expanded and includes informative text and charts on the relationship of electronic orbitals and complex formation.

The other chapters of the theoretical section cover atoms, molecules, and solubility; electrolytes; atomic and molecular structure; oxidation-reduction equations; oxidation-reduction equilibria; equilibrium and reaction velocity; equilibria of weak acids and bases; the Brønsted concept of acidity; solubility product; colloidal properties; polybasic acids; hydrolysis, acid-

base equilibria, buffers; amphoteric substances. A brief introduction to laboratory techniques follows the theoretical section.

The qualitative scheme covers only a limited selection of common metallic ions and anions. The group separations for the metallic elements are familiar ones, essentially along lines of the Noyes and Bray scheme. The anion scheme utilizes group tests, for example, for oxidizing or reducing properties, and for precipitation by barium, silver, or calcium ions, to narrow the field of specific tests for the limited selection of anions that is provided for in the scheme.

The appendix includes lists of apparatus and reagents, density-molarity tables for the common acids and ammonia, preparation of test solutions, and mathematical operations and problems thereon. Further tables are for ionization constants of weak acids and bases, solubility products, dissociation constants of complexes, and a very extensive table (32 pages) of properties of substances that may be formed by combinations of the various anions and cations that are provided for in the qualitative schemes.

The subject index is rather brief, but probably adequate. Tables of four-place logarmithms and a set of answers to problems follow the index. A table of 1953 atomic weights is inside the front cover, and a periodic chart, including transuranic elements, is inside the back cover. The typography and the figures are excellent.

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The Properties of Glass. George W. Morey. ACS Monograph Series No. 124. William A. Hamor, Ed. Reinhold, New York, ed. 2, 1954. 591 pp. Illus. $16.50.

Morey's definitive book on glass properties follows closely the format and organization of the 1938 edition and it remains the best available book on the subject. During the past 15 years this book has achieved first rank in providing reliable information to glass technologists and scientists interested in glass. The emphasis on reliability of property data in relation to chemical composition, especially Morey's own pioneering and continuing work on phase equilibriums, has contributed greatly to the development of systematic research in glass. While some of its shortcomings may be minor, they nevertheless deserve to be considered here.

The first three chapters cover the chronological development and characteristics of glass, crystallization studies of glass systems and rates of crystal growth, and the requirements of commercial glasses and the development of new compositions. The presentation would have been improved if glass history and statistics had been brought up to date and a more complete coverage of devitrification rate studies had been included.

Chapter 4 covers the chemical resistance characteristics important in glass usage. It is believed that the four new references do not adequately cover the chemical durability studies made since 1938.

The next 16 chapters are devoted to specific glass properties important in glass fabrication and end usage. Some 225 references are made to new material in these chapters, and many new data have been added. Discussions on new material appear to have been added in a manner that least disturbs the original format. This has resulted in overcondensation and, in a few instances, near exclusion of some accounts of new property measurements.

The last chapter discusses the constitution and structure of glass, principally on the basis of x-ray diffraction studies. Many investigators will not agree with the author's implication that x-ray diffraction studies, notably the excellent work of Warren and his coworkers, give a satisfactory picture of glass structure. In fact, in the author's reference No. 57 to this work, Warren states (p. 258):

> . . . the X-ray diffraction study of a glass gives information only on average quantities; it tells nothing about the fine details of the structure. . . . The X-ray studies of glass might be said to establish the first order approximation to a picture of the structure, and the fine details must be filled in with other kinds of measurements.

Although future research may show that this average picture is the best that can be achieved, I would point out that it is too indefinite to be of much use except in the most simple problems of glass technology. A complete account should have included the continuing efforts of many investigators to apply Raman and infrared spectra, heat capacity, neutron and electron diffraction, electron microscope, and other types of data toward a more definite and usable picture of glass structure.

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The Steel Skeleton. vol. I. *Elastic Behaviour and Design.* J. F. Baker. Cambridge Univ. Press, New York, 1954. xi + 206 pp. Illus. + plates. $8.50.

In 1929 the British steel industry and the Department of Scientific and Industrial Research helped form the Steel Structures Research Committee and embarked upon an intensive investigation of various design procedures applicable to steel building frames. It was believed by many engineers that the ductile properties of steel were not fully exploited for structural purposes and that existing building codes were irrational and too restrictive. It was hoped that certain advantages would exist in a design procedure based on the theory of continuous frames and on the ductile properties of steel.

Volume I of *The Steel Skeleton*, by J. F. Baker of Cambridge University, is a review of the analytic and experimental investigations that were conducted by the Steel Structures Research Committee on the elastic behavior of steel building frames. Volume II

is to be called *Plastic Behaviour and Design* and is to describe the investigations pertaining to the inelastic ranges of loading.

The first two chapters of volume I present a summary of the specifications and practices that existed in various countries at the time the Steel Structures Research Committee was formed. Differences were observed in the specified live loads, wind loads, working stresses, and column formulas. The procedure indicated for checking the proportions of beams and columns was common to most building codes. For gravity loads, the beams were to be checked as simply supported beams and the columns were to be checked as pin-ended columns with or without eccentric loads. Provisons for continuity of columns were usually in the form of "effective lengths."

The next five chapters deal with the experimental phases of the investigation and present the results of tests on an experimental frame and three actual building frames. Various stiffnesses of beam-to-column connections were considered. These ranged from light beam connections, as in the experimental frame, to exceptionally stiff connections, as in a hotel building. Strains were measured for the various stages of construction ranging from the bare frames to the frames with floors laid and columns encased. It was observed that the behavior of an actual building was radically different from that assumed in the design methods in common use. The behavior was closer to that of a rigidly jointed frame than to that of a structure with hinged-ended beams. The columns had appreciable bending, and even comparatively light beam connections transmitted much heavier bending moments than had been anticipated.

The results of tests concerning the moment-angle change relationships for various types of beam-to-column connections are presented. These results are used in interpreting the behavior of the actual building frames, in developing several analytic procedures for frames with semirigid connections, and in developing a design method for such frames. Various conditions of loading and different types of frames were considered in arriving at a set of recommendations for the design of beams and columns in building frames. In the recommendations for the design of beams, allowance is made for the restraining moments at the ends of the beams. Adjusted standard curves are presented for different connections to maintain constant load factors, even though the design is based on working loads and working stresses. In studying the critical loading conditions causing single curvature or double curvature of columns, the yield stress of the material is used as a criterion of failure. As might be expected, the moments in the columns are large and extremely sensitive to the loading conditions considered. The book includes a summary of the recommendations made by the Steel Structures Research Committee in regard to the design of steel building frames.

In conclusion, the author discusses the reception of the recommendations given by structural designers and organizations involved in codifying practice. In general, a reluctance has been shown in modifying existing codes and rules of practice. This reluctance is principally due to the complications that are involved in the recommended design procedure without such complications being offset by a reduction in the amount of steel required in a building frame. Provided that no adjustments are made in load factors, the recommended design procedure, although rational, leads to lighter beams but heavier columns than ordinarily called for. The author indicates that volume II is to deal with a simpler method of design based on the plastic behavior of structures.

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Biographical Memoirs. vol. XXVIII. National Academy of Sciences, Washington, D.C., 1954 (Order from Columbia Univ. Press, New York). 311 pp. Plates. Paper, $4.

This volume includes notices of Francis G. Blake by John Rodman Paul, of Gano Dunn by Vannevar Bush, of Merritt L. Fernald by Elmer D. Merrill, of Frederick P. Gay by A. R. Dochez, of E. B. Hart by Conrad A. Elvehjem, of Ludvig Hektoen by Paul R. Cannon, of Raymond A. Kelser by Richard E. Shope, of Elmer A. Sperry by J. C. Hunsaker, of George L. Streeter by George W. Corner, and of Frank C. Whitmore by C. S. Marvel. The biographies are as various as their diverse subjects and authors. Perhaps the single quality they share in common is their ability to move the reader to unbounded admiration for the energy, industry, imagination, and humanity of the men they portray. These men were all born, roughly, within the last third of the 19th century, and they have all contributed greatly to the vigor of present American thought. The facts of their lives constitute the raw material of contemporary intellectual history, and for this reason, as well as for the sake of commemorating these individuals from a personal point of view, the volume is fascinating to read.

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Coronary Heart Disease in Young Adults. A multidisciplinary study. Menard M. Gertler and Paul D. White. Harvard Univ. Press, Cambridge, 1954 (For the Commonwealth Fund). xviii + 218 pp. Illus. + plates. $5.

This monograph represents the result of a concerted effort of nine well-known researchers and cardiologists trying to explain why some young persons are singled out and die following an acute coronary episode. Even a few of the conclusions give impressive evidence of the results of this study:

1) Coronary heart disease is more likely to occur if parents or siblings have experienced the disease.

2) The disease is associated more with a specific body build (the fat, muscular type) than with an increase of body weight.

3) The coronary patients are physically more masculine than the controls but are psychologically more feminine, possibly because of their cultural background.

4) The coronary patients are slightly hypothyroid.

5) Coronary heart disease can exist without hypercholesterolemia, even though this is often present; the predisposition is more important than any other factor.

The book is well arranged and its reading is easy and pleasant. The only criticism that can be made is the limitation to a small number of patients (100 cases) and the scarcity of patients of certain racial groups. This decreases the statistical value of the study. In spite of this, the monograph represents an important step in the slowly growing mass of knowledge about coronary heart disease.

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Vegetable Tanning Materials. F. N. Howes. Chronica Botanica, Waltham, Mass.; Butterworths, London, 1953. xi + 325 pp. Illus. $5.50.

A cheerful soul may find the world a good place to live in and may find that trees have wholesome personalities. The vegetable tanning materials are characters that have been important for thousands of years in converting raw hides, which are almost as unstable as meat, into durable leather.

Native plants found in different parts of the world contain enough tannic acid, or similar compounds, to be useful in local tanning, and during the last 100 years tanning materials have become an important part of world trade.

Commercial extracts have been developed from barks, fruits, leaves, roots, plant galls, and even woods. They may be liquid, solid, or spray-dried powder. Evaporation is done under a vacuum or as a spray, because the less heating required, the greater the preservation of useful organic compounds.

Vegetable Tanning Materials authoritatively covers the 39 commercial vegetable tanning materials of the world, together with outlines of the processes for the manufacture of extracts and for vegetable tanning. Also discussed are the sizable world trade in these materials and the biology of the tannins. Other tanning materials than vegetable are indicated. The 16 illustrations and the 10 figures add to the reading interest. There are references to other works and a list of the botanical names.

The three materials (extracts) used throughout the world in largest tonnages are mimosa or wattle bark, which is cultivated on plantations in South Africa and Australia; quebracho wood, a slow-growing tree scattered through forests in the Argentina-Paraguay area; and chestnut wood from the mountain regions of the southern United States, France, and Italy. Hemlock and oak barks have been replaced by these three items. Chestnut trees in the United States seem to be doomed by a blight, but the dead trees can be used along with the remaining live ones.

Of increasing importance is the bark of the mangrove tree, which grows in tropical swamps where rivers mix with salt water. Among other tanning materials covered and in general use are myrabolans, a dried fruit from India; sumac leaves from Sicily; acorn cups from Turkey, and divi-divi pods from tropical America.

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Crystal Data. Classification of substances by space groups and their identification from cell dimensions. J. D. H. Donnay and Werner Nowacki. Memoir 60. Geological Society of America, New York, 1954. ix + 719 pp. $5.

This important and stimulating volume consists of two independently prepared and essentially unrelated tabulations of crystal data.

Part I, by Nowacki, consists of a listing by space group and general chemical nature of 3782 structures reported in the literature prior to July 1948. The purpose of this listing is to provide statistical data on the distribution of crystal structures among the 219 possible symmetrical packing arrangements that are permitted by our geometry. Nowacki refers in his preface to some preliminary use that he has made of this material in trying to understand one of the great unsolved problems of crystallography: Why does a particular chemical entity in a particular thermodynamic state pick one type of crystal packing rather than any other? Very little progress has been made in the understanding of this problem, but the present tabulation takes an important preliminary step.

Tables 1–6 represent numerical analyses of the data of the main table of part I. From these tables it is clear that nature concentrates on only a few of the many space patterns available to it. For 41 space groups no structures have been reported, while in 32 groups only one appears. Only 10 space groups have individually more than 3 percent of all structures, and together these 10 groups contain about 46 percent of all structures.

When one narrows the chemical classification, the figures become even more striking. In the inorganic structures, again 10 space groups contain more than 3 percent of the structures reported, and together these groups contain about 50 percent of the structures of this type. In the organic structures, only eight space groups have more than 3 percent and together these eight groups account for 60 percent of the structures. The three most popular space groups account for 43 percent of all organic structures. A final example concerns the aromatic and heterocyclic molecules which are often flat and are, therefore, particularly attractive to crystallographers. In this category, eight space groups contain more than 3 percent of all

structures, and together they contain 72 percent of all structures; one space group alone contains 42 percent of all structures. In the heterocyclic compounds taken alone, this same space group accounts for 54 percent of all structures, and only three other groups contain more than 3 percent.

The discussion of part I is best closed by a misquotation of parts of the preface:

> Let us hope . . . that . . . the present statistical survey . . . will incite theoreticians to search for an explanation of the facts which it has brought to light.

Part II of *Crystal Data*, prepared by Donnay with the collaboration of many others, represents a major improvement on an already standard and essential tool of analytic chemistry. The powder method of identification of pure substances is used in thousands of scientific and industrial control laboratories throughout the world. With this very powerful method, one can very often achieve an identification of an unknown material, but in doing so one uses only a few of the facts that can be gleaned from a study of a single crystal. With modern single-crystal methods, it is very easy to determine the cell dimensions and the space group for an unknown material. If these data for the material have been previously recorded in a file, the unknown can be identified with much greater certainty than is possible with the powder method. The present work is an attempt to provide such a file. Single-crystal data from an unknown material can be reduced by a standard procedure to a form that can be used to determine whether or not the substance in question has been listed. If it has been listed, the identification can be complete; if it has not been listed, the unknown is an interesting subject for an x-ray analyst.

The joint preface and the introductions to the sections disarm a reviewer who wants to be too critical. Both authors acknowledge with admirable candor their fallibility and indicate to the reader by their indexing technique the way in which this can be detected. From the point of view of accurate coverage of the published material, the two parts, separately and combined, leave much to be desired. In the future, no literature search should start without reference to this book, but unfortunately such a search cannot end here.

The authors and their collaborators are to be congratulated and commended for their contribution to the literature of crystallography despite the shortcomings of their work. Unfortunately, they cannot be expected to continue indefinitely in this tedious operation, and it is hoped that the International Union of Crystallography will be able to arrange for a collaborative effort to maintain these two important classifications.

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Books Reviewed in THE SCIENTIFIC MONTHLY

November

The Psychology of the Criminal Act and Punishment, Gregory Zilboorg (Harcourt, Brace). Reviewed by D. W. Louisell.

Causality in Natural Science, Victor F. Lenzen, (Thomas). Reviewed by A. Rapoport.

Nobel Prize Winners in Chemistry: 1901–1950, Eduard Farber (Schuman). Reviewed by R. Adams.

Know Your Reader, George R. Klare and Byron Buck (Hermitage House). Reviewed by J. W. Hedgpeth.

A Field Guide to the Birds of Britain and Europe, Roger Tory Peterson, Guy Mountfort, and P. A. D. Hollom (Houghton Mifflin). Reviewed by C. H. Rogers.

The Climates of the Continents, W. G. Kendrew (Oxford Univ. Press, ed. 4). Reviewed by H. P. Bailey.

Personality through Perception, H. A. Witkin, H. B. Lewis, M. Hertzman, K. Machover, P. Bretnall Meissner, and S. Wapner; Gardner Murphy, Ed. (Harper). Reviewed by S. C. Ericksen.

The Natural History of Mammals, François Bourlière (Knopf). Reviewed by F. A. Pitelka.

Proceedings of a Conference on the Utilization of Scientific and Professional Manpower and ***Policy for Scientific and Professional Manpower,*** National Manpower Council (Columbia Univ. Press). Reviewed by H. A. Armsby.

Insecticides and Colonial Agricultural Development, T. Wallace and J. T. Martin, Eds. (Butterworths). Reviewed by B. B. Pepper.

Number: The Language of Science, Tobias Dantzig (Macmillan, ed. 4). Reviewed by E. T. Bell.

Basic Bacteriology, Carl Lamanna and M. Frank Malette (Williams & Wilkins). Reviewed by P. Gerhardt.

Religion, Philosophy and Psychical Research, C. D. Broad (Harcourt, Brace). Reviewed by F. P. Clarke.

Music Therapy, E. Podolsky, Ed. (Philosophical Library). Reviewed by P. R. Farnsworth.

Pattern of the Tiger, Stanwell Fletcher (Little, Brown). Reviewed by D. Bidney.

Organic Chemistry, Robert Ward Getchell (McGraw-Hill). Reviewed by C. A. VanderWerf.

Plant Breeding for Everyone, John Y. Beaty (Charles T. Branford). Reviewed by G. W. Dillon.

Practical Chromatography, R. C. Brimley and F. C. Barrett (Reinhold; Chapman & Hall); ***Chromatographic Methods of Inorganic Analysis,*** F. H. Pollard, and J. F. W. McOmie (Academic Press; Butterworths). Reviewed by J. H. Yoe.

Man, Rockets and Space, Burr W. Leyson (Dutton). Reviewed by H. S. Tsien.

Viruses, Cold Spring Harbor Biological Laboratory. Reviewed by G. H. Bergold.

A History of The College of Pharmacy, Columbia University, Charles W. Ballard (Columbia Univ. Press). Reviewed by G. L. Jenkins.

The Hand Produced Book, David Diringer (Philosophical Library). Reviewed by J. Holmes.

Industrial Electronics, R. Kretzmann (Philips Technical Library; Elsevier). Reviewed by B. R. Gossick.

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Freaks and Marvels of Insect Life. Harold Bastin. Wyn, New York, 1954. 248 pp. Illus. + plates. $3.75.

Foreign Policy Analysis. Feliks Gross. Philosophical Library, New York, 1954. xxiv + 179 pp. $3.75.

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Enfermedades Infecciosas y Parasitarias. vols. 1 and 2. Jose Ink. Lopez & Etchegoyen, Buenos Aires, 1953. xxvii + 1485 pp. Illus. + plates.

Careers and Opportunities in Science. A survey of all fields. Philip Pollack. Dutton, New York, 1954. Revision of *Careers in Science*. 252 pp. Plates. $3.75.

A Treatise on Electricity and Magnetism. vols. I and II. James Clerk Maxwell. Dover, New York, 1954. An unabridged reprint of the last rev. ed. 3 (1891). vol. I, xxxii + 506 pp.; vol. II, xxiv + 500 pp. Illus. + plates. $4.95.

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The Study of the Brain. A companion text to the stereoscopic atlas of neuroanatomy. Hyman S. Rubinstein. Grune and Stratton, New York, 1953. xiii + 209 pp. Illus. + plates. $9.50.

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The Story of Man. From the first human to primitive culture and beyond. Carleton S. Coon. Knopf, New York, 1954. xxii + 437 pp. Illus. + plates. $6.75.

Packaging Engineering. Louis C. Barail. Reinhold, New York, 1954. vii + 407 pp. Illus. $9.50.

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General Education: Explorations in Evaluation. The final report of the cooperative study of evaluation in general education of the American Council on Education. Paul L. Dressel, director. American Council on Education, Washington, D.C., 1954. xxiii + 302 pp. $3.50.

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Technical Papers

Presence of Carbohydrates Distinct from Acid Mucopolysaccharides in Connective Tissue

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Previous studies of connective tissue indicated that purified skin collagen (*1*), cornea (*2, 3*), lens capsule (*4*), cartilage (*5*), and bone (*6–8*) contained one or more of the three aldoses—galactose, glucose, and mannose. Recently, we identified these three aldoses and also fucose in chromatograms of hydrolysates of four tissues rich in reticular fibers and basement membranes (*9*). In the present study (*10*), a technique originally devised to separate aldose-containing material from the organic portion of bone (*11*) was applied to several connective tissues obtained from cattle, namely (i) the lung, an organ rich in reticular fibers and basement membranes; (ii) Achilles tendon and the derma of the skin, two structures rich in collagenous fibers; (iii) the ligamentum nuchae, an elastic tissue; and (iv) tracheal cartilage and bone matrix, two connective tissue derivatives.

The lung was prepared by forcing water through the arteries to remove blood and through the bronchi to remove mucus; the pleura was stripped off, and the main blood vessels and bronchi were excised. Tendon, ligamentum nuchae, and cartilage, which are essentially avascular, were merely freed of all adhering tissue. To prepare bone matrix, the compact portions of femurs were decalcified with 0.15 percent hydrochloric acid (*12*). All these tissues were extracted with 0.5*N* sodium hydroxide for 4 days in the cold, and the neutralized extracts were treated with 2 vol of alcohol to precipitate out acid mucopolysaccharides (*13, 14*). This precipitate is referred to as fraction I. On increasing the alcohol concentration to 84 percent, a second precipitate was obtained (fraction II). An attempt was made to eliminate proteins from the two fractions by successive treatments with a chloroform-amyl alcohol mixture and with Lloyd's reagent (*13, 14*). The yields of fraction II were higher than those of fraction I in all the tissues examined except cartilage (Table 1).

As another type of connective tissue derivative, the capsule of the lens was also studied. The capsules were stripped off the lenses, wiped with a cloth on both surfaces to remove adhering material, washed for several hours in water to eliminate soluble substances, and dried.

Fifty milligrams of fractions I and II from each tissue under study and of the lens capsule were hydrolyzed for 2 days at 100°C in the presence of a cation exchange resin (*9*), and the hydrolyzates were analyzed by paper chromatography for the identification of the monosaccharide units (*9, 15*).

Fraction I from each one of the afore-mentioned tissues contained glucuronic acid (*16*). This result was expected, since fraction I had been prepared by a precipitation procedure that is known to yield acid mucopolysaccharides (*13, 14*) and, therefore, should contain glucuronic acid. Indeed, acid mucopolysaccharides had already been extracted from the lung (*17*), tendon (*18*), skin (*13, 14*), ligamentum nuchae (*19, 20*), cartilage (*5, 18*), and bone (*6, 19, 21*).

Fraction II from any one of the tissues, as well as the whole lens capsule, contained no glucuronic acid. Galactose, mannose, and fucose were invariably present (Fig. 1). In addition to these aldoses, glucose was identified in some of the preparations. It is of interest that the carbohydrate pattern of fraction II from lung was identical to that previously described as characteristic of reticular fibers and basement membranes (*9*). The fraction II from tendon yielded a different carbohydrate pattern, presumably characteristic of the collagenous fibers of which this tissue is composed. From the method of isolation of fraction II, it can be concluded that the aldoses are not present in the form of free monosaccharides but rather are combined as constituents of larger molecules. Furthermore, the nitrogen content of fractions II (10 to 15 percent) suggests that large amounts of protein are associated with these extracts. These materials may consist of a mixture of substances, but no attempt has yet been made to characterize them according to homogeneity, purity, or chemical composition other than by the chromatographic technique described.

In a parallel histochemical study, Orth-fixed sections of the cattle tissues under investigation here were stained by the periodic acid-Schiff technique for the detection of carbohydrates containing free 1,2-glycol (and α-amino alcohol) groups (*22*). The lens capsule reacted intensely; the cartilage and bone matrix, moderately. The collagenous fibers in the derma stained weakly, whereas those in the tendon did not stain at all. However, when sections of derma and tendon were treated with a commercial sample of "pectinase" before applying the periodic acid-Schiff technique, the col-

Table 1. Yields of the fractions, in percentages of dry weight, obtained from various types of connective tissue and derivatives.

	Fraction I (rich in glucuronic acid)	Fraction II (rich in aldoses)
Elastic tissue (ligamentum nuchae)	0.1	0.3
Tendon (Achilles)	.2	> 2.0
Lung (framework)	.7	5.6
Skin (derma)	.3	6.8
Cartilage (tracheal)	14.8	3.5
Bone (compact femoral)	0.2	2.4

lagenous fibers stained intensely (*23*). In ligamentum nuchae, the elastic fibers did not stain, whether or not pectinase was used; but the interstitial material separating the fibers stained weakly before, and intensely after, pectinase treatment. Thus, a fraction II could be extracted from all sites that reacted with the periodic acid-Schiff technique either directly or after treatment with pectinase. In fact, when the fractions were subjected to the periodic acid-Schiff spot test devised by McManus and Hoch-Ligeti (*24*), the fractions II were intensely reactive, whereas the fractions I were not reactive. It was concluded, therefore, that the carbohydrate moiety of the various fractions II was responsible for the periodic acid-Schiff reactivity of connective-tissue structures.

In conclusion, the chemical investigation of a number of connective tissue structures (which stain with the periodic acid-Schiff technique either directly or after pectinase treatment) led to the isolation of carbohydrate-containing materials that are distinct from the acid mucopolysaccharides, since they invariably contain galactose, mannose, and fucose but are free of glucuronic acid.

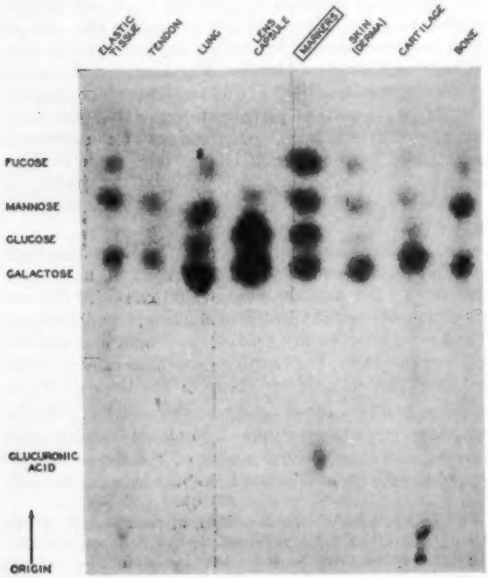

Fig. 1. Chromatographic pattern of the monosaccharides present in fraction II of various types of connective tissue and derivatives as well as in the capsule of the lens. The chromatograms were developed three times in a butanol-pyridine-water solvent (*25*) and were sprayed with aniline hydrogen oxalate (*26*). The markers (5th column) are labeled on the left-hand side. Galactose and mannose are visible in all samples. Fucose was also present in all hydrolyzates, but in some cases the spots were too faint to reproduce clearly in the photograph. (Although in this composite chromatogram the spots deviated slightly from those of the markers, individual chromatograms of each fraction showed an exact correspondence.)

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29 June 1954.

Errors in the "Isopiestic" Method for Measuring Masses of Salt Particles

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An "isopiestic" method has been applied by Woodcock and Gifford (*1*) and others to measurement of the sizes of atmospheric sea salt particles. The method consists essentially of measuring the equilibrium diameters of hemispherical water droplets containing the dissolved salt particles when exposed to a known water vapor pressure. The mass of salt in each droplet is calculated on the basis of the experimental relationship between salt concentration and equilibrium vapor pressure. The droplets sizes usually are in a range where the Thomson-Gibbs effect of curvature can be neglected.

I have performed several series of isopiestic experiments (*2*), using a small metal test chamber, in which droplets of NaCl solution were supported on surfaces

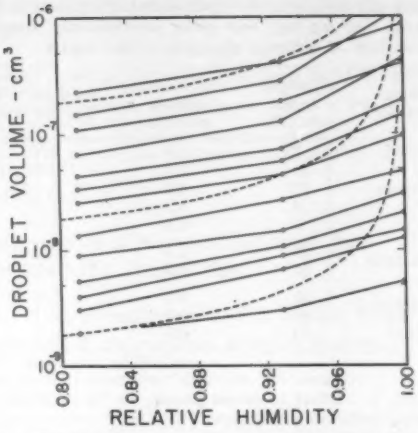

Fig. 1. Relationship between droplet volume and relative humidity for hemispherical droplets of NaCl solution on a Dri Film surface. Solid lines, experimental; dashed lines, calculated.

of Teflon or of glass coated with Dri Film SC-87 (*3*). Both of these surfaces give contact angles very close to 90°, so that the droplets were practically hemispherical. Diameters of the droplets were measured by a microscope, looking through a window in the top of the test chamber. A number of droplets were measured at three values of relative humidity, 1.00, 0.930, and 0.811, maintained by a small tray containing, successively, water, a saturated $(NH_4)H_2PO_4$ solution, and a saturated $(NH_4)_2SO_4$ solution. These solutions were chosen because they maintain relative humidity practically independent of temperature (*4*) in the region of the temperature used (25°C), thus eliminating the need for precise temperature control. After closure of the small chamber, equilibrium was reached essentially in 15 to 20 min for the smaller droplets and in about 1 hr for the largest droplets used. No measurable change in droplet size occurred thereafter in times ranging up to several days.

Representative experimental data are shown in Fig. 1, where the hemispherical droplet volumes are plotted as a function of the relative humidity. The experimental points are shown as circles; the solid lines join points applying to the same droplet. The data shown were taken with the droplets on a Dri Film support, but closely similar results were found with the Teflon support.

For comparison, calculations were made of droplet volume versus relative humidity for three NaCl masses, 5×10^{-10}, 5×10^{-9}, and 5×10^{-8} g, using the *International Critical Tables* data (*5*) for equilibrium concentration versus relative humidity and (*6*) for solution densities. The results are shown as the three dashed curves in Fig. 1. The theoretical curves are asymptotic to the line RH = 1.00 if the Thomson-Gibbs effect is neglected; inclusion of the Thomson-Gibbs effect makes no appreciable difference within the range of the graph but causes the curves to intersect RH = 1.00 several decades above the top of the graph.

Rough measurements of the sizes of the solid NaCl particles left after complete evaporation of the droplets indicate that the NaCl contents of droplets measured at 0.811 relative humidity are probably within a few percent of those calculated by the method used for the theoretical curves. The discrepancy between the forms of the experimental and theoretical curves indicates, however, that at 0.93 relative humidity the mass of NaCl will be underestimated by about 20 percent; at 0.96 relative humidity it probably will be underestimated by about 35 percent.

Although the present measurements refer to NaCl only, it is expected that similar results will be found with other salts. Errors of the afore-mentioned magnitudes may not be very important, of course, in some applications of the isopiestic method. But if it is necessary that errors be kept down to a few percent, humidities apparently should be used that will result in near-saturation of the droplets.

No satisfactory explanation has been found for the apparent difference in vapor pressure behavior between the solution in small hemispherical droplets and in larger, more or less plane, areas. It might be suspected that the discrepancy is due to a decrease in the surface free energy in the neighborhood of the 90-deg contact with the supporting surface; if this is true, it would be expected that continual convection would exist within the droplets, accompanied by gradients of concentrations and temperature. Microscopic observation of suspended particles in the droplets indicates, however, that such convection is not present.

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24 June 1954.

On the Protection against Alloxan Diabetes by Hexoses

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In earlier communications (*1*, *2*) it was reported that preadministration of glucose, mannose, and fructose but not of galactose protected animals from diabetes caused by alloxan. Administration of the sugars after alloxan, however, had no protective action. Evidence for any direct reaction between glucose and alloxan could not be obtained (*1*). From these results, it was suggested that inhibition of beta cell hexokinase by alloxan was possibly the primary step in the dia-

betogenic action of alloxan (*2*). This paper reports the results of an extension of the earlier studies.

Overnight-fasted rats (weight 100 to 150 g) were the animals used. Presence or absence of diabetes was judged as before (*2*).

None of the following sugars and sugar-derivatives given intravenously before a 40-mg/kg intravenous dose of alloxan offered any protection from diabetes: sucrose (5 g/kg), lactose (5 g/kg), D-xylose (5 g/kg), D-arabinose (5 g/kg), L-arabinose (5 g/kg), D-sorbitol (5 g/kg), D-mannitol (5 g/kg), and Na-gluconate (3 g/kg). Maltose (5 g/kg), however, offered protection in all the animals.

The evidence of protective abilities of the sugars, as obtained by the method of preadministration so far followed, was to some extent vitiated owing to the possibility of interference by intermediate breakdown products of the sugars actually administered. In the present series of experiments, therefore, alloxan and the sugar tested were given simultaneously, the alloxan being dissolved in solutions of varying strengths of the sugar tested. Only the sugars that offered protection when given before alloxan—that is, glucose, mannose, fructose, and maltose—were used in these experiments. The results are given in Table 1.

Thus, the ability to protect animals against diabetes caused by alloxan is probably limited to glucose, mannose, and fructose. Their relative protective abilities as judged from 100 percent protection (Table 1) are approximately: glucose : mannose : fructose = 100 : 50 : 15. The protection given by preadministered maltose possibly resulted from glucose produced *in situ* from the maltose.

Table 2 gives the results of the effects of alloxan on succinic oxidase in both the presence and the absence of excess glucose. The succinic enzyme was prepared from pigeon breast muscle by the method of Barron and Kalnitsky (*3*). The results show that the previous presence of excess glucose did not affect the action of alloxan on the succinic enzyme. This confirms the view, earlier expressed from chemical evidence (*1*), that protection against alloxan diabetes by the hexoses is not the result of any direct reaction between the hexoses and alloxan leading to the inactivation of the latter.

The relative protective abilities of the hexoses against alloxan diabetes as described here closely simulate their relative affinities to the ordinary mammalian hexokinase. In view of the hexokinase inhibition theory of alloxan action (*2*), this suggested that the antagonism between the hexoses and alloxan was possibly competitive in nature. Table 3 gives the results of experiments undertaken with a view to obtain *in vivo* information on the point.

The results show (Table 3) that the protection against a given dose of alloxan by a certain dose of glucose could be overcome by increasing the dose of the alloxan used and that the diabetogenic effect of the increased dose of alloxan could again be counteracted by further increment in the dose of the glucose. In view of the fact that alloxan and glucose do not react with each other, the results indicate that the antagonism between glucose and alloxan with respect to the development of diabetes in animals is possibly competitive in nature.

Thus, we believe that the results reported here add further strength to the hexokinase inhibition theory of alloxan action. The competitive nature of the antagonism between glucose and alloxan also possibly throws more light on the selectivity of alloxan for the beta cells.

Table 1. Effect of simultaneous administration of sugars and alloxan on the development of diabetes in rats. Alloxan (40 mg/kg) was given intravenously dissolved in solutions of different strengths of the sugars.

Sugar tested	Strength sugar soln. (%)	Strength alloxan soln. (%)	No. diab. rats/ No. rats used
D-glucose	7	1.0	6/6
	11	1.0	2/8
	12	1.0	0/10
	6	0.5	2/8
	7	0.5	0/10
D-mannose	22	1.0	2/6
	25	1.0	0/10
D-fructose	35	0.5	2/6
	40	0.5	0/10
Maltose	50	0.5	6/6

Table 2. Effect of excess glucose on the inhibition of succinic oxidase by alloxan.*

Contents of vessels during test	Oxygen uptake (μL O_2/30 min)
Enzyme alone (no succinate)	0
Enzyme + glucose (no succinate)	0
Enzyme + succinate	211
Enzyme + glucose + succinate	215
Enzyme + alloxan + succinate	71
Enzyme + glucose + alloxan + succinate	72

* Enzyme activity was measured manometrically by the Warburg apparatus. Each vessel contained 0.4 ml of enzyme, 0.1*M* phosphate buffer, pH 7.4, 0.2 ml of 10 percent glucose (or 0.2 ml of distilled water) and 0.2 ml of 0.5 percent alloxan monohydrate (or 0.2 ml of distilled water); 0.1 ml of 1*M* succinate was added from the side bulb immediately after the first reading (15 min after the addition of alloxan). Total volume, 2 ml; gas-air, temp., 38°C; duration of experiment, 30 min.

Table 3. Effect of increased doses of alloxan on glucose-protection against alloxan diabetes in rats. Alloxan was given intravenously dissolved in solutions of glucose of varying strengths.

Dose of alloxan (mg/kg)	Strength alloxan soln. (%)	Strength glucose soln. (%)	No. diab. rats/ No. rats used
40	1.0	12	0/10*
50	1.25	12	6/6
50	1.25	18	0/10
60	1.5	18	6/6
60	1.5	25	0/10

* Reproduced from Table 1.

I wish to express my gratitude to B. B. Sarkar and P. B. Sen for their encouragement and interest in this study.

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7 July 1954.

Detection of a New Inhibitor of the Tricarboxylic Acid Cycle

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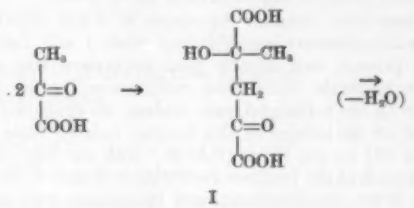
Comparison of different samples of sodium pyruvate (commercial and prepared in this laboratory) showed the presence of variable amounts of a substance that was correlated with an altered behavior of rat heart mitochondria in the oxidation of pyruvate (*1*). The mitochondrial suspension oxidized pure pyruvate completely when small amounts of malate were added, with an oxygen-to-pyruvate ratio of the theoretical value of 5, the tricarboxylic acid cycle being self-perpetuating and operating at an initial Q_{O_2} of between 800 and 1000. Each member of the cycle initiated the oxidation of pyruvate by acting as an oxalacetigen (*2*). However, using a pyruvate containing the impurity, a different pattern of metabolism was exhibited: (i) The cycle was no longer self-perpetuating and, for the utilization of all the pyruvate, an equimolar amount of malate was required; (ii) the oxygen-to-pyruvate ratio dropped to a value arund 3; (iii) the tricarboxylic acids (citrate, cis-aconitate, and isocitrate) no longer acted as oxalacetigens; and (iv) a ketonic substance accumulated as the pyruvate was utilized, the conversion being quantitative. The incorporation of pyruvate into the cycle was not affected by this impurity, as was indicated by the fact that no change was observed in the initial Q_{O_2}. The spectral absorption curve of the 2,4-dinitro-phenylhydrazone of the accumulated substance corresponded quite closely to that of the similar derivative of α-ketoglutarate, and the accumulated substance, therefore, was temporarily assumed to be α-ketoglutarate.

This impurity was found to be present in commercial pyruvic acid and in certain samples of sodium pyruvate prepared from triply redistilled pyruvic acid according to the standard procedure (*3*). Pyruvic acid, originally 99-percent pure, contained no more than 25 percent pyruvic acid after 1 to 2 years. When such pyruvic acid was redistilled under reduced pressure (10 mm-Hg), a fraction distilled over at a higher temperature (105° to 108°C) than the pyruvic acid fraction (55° to 58°C). The higher boiling fraction was a viscous fluid at room temperature from which a waxy crystalline mass slowly formed in the cold, and both liquid and solid material produced the same type of block in the cycle as was previously demonstrated with the impure samples of sodium pyruvate. Sodium pyruvate prepared from triply redistilled pyruvic acid sometimes contained the sodium salt of this impurity in sufficient amounts to produce marked cycle block. Depending on the purity of the original pyruvic acid and the conditions of crystallization of the sodium pyruvate, as much as 25 percent impurity was found in the final product.

A sample of sodium pyruvate containing the impurity was examined by paper chromatography, and it was found that the impurity migrated at approximately the same rate as the pyruvate, indicating that it was a monocarboxylic acid under these conditions. Pyruvate treated for 3 days with 1*N* hydrochloric acid inhibited the oxalacetigenic action of citrate in the mitochondrial preparation 65 percent. It was concluded that the impurity was formed from pyruvic acid. It is known that pyruvic acid is capable of slowly forming a dimer (γ-methyl-γ-hydroxy-α-ketoglutaric acid, I) and that this dimer may lose water to form the cyclic α-keto-γ-valerolactone-γ-carboxylic acid (II). The lactone, furthermore, is believed to exist in a keto-enol equilibrium (II, III). It was considered that



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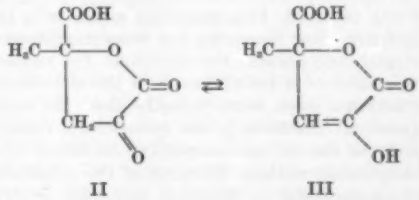

II III

any one of these substances might be involved in the mitochondrial block observed. We therefore prepared the lactone by a method (*4*) in which hydrochloric acid gas was passed for 9 days through a long column of pure, triply redistilled pyruvic acid; the final viscous liquid was allowed to stand over concentrated sulfuric acid in vacuum for 3 days, and a mass of waxy, highly hygroscopic, crystalline material was obtained. The prepared lactone was found to be a potent blocker of the tricarboxylic acid cycle in rat heart mitochondria and, when added with pure pyruvate, produced all the phenomena described here, namely, the failure of the cycle to be self-perpetuating, the inability of the tricarboxylic acids to act as oxalacetigens, and the accumulation of a substance temporarily identified as α-ketoglutarate. The inhibition of the ability of citrate and isocitrate to function as oxal-

acetigens was pronounced at concentrations of lactone as low as $1 \times 10^{-5} M$. The time curves of oxygen uptake during pyruvate oxidation illustrated the blocking action (which prevents the self-perpetuation of the cycle) of the impurity and the prepared lactone; the oxidation of pure pyruvate proceeded at a fairly steady level until completion, whereas with impure pyruvate or in the presence of the lactone the rate suddenly fell to a low level when the small quantities of malate had been utilized. Neither the oxidation nor the oxalacetogenic ability of succinate was inhibited by the lactone.

These results might be interpreted to mean that this potent inhibitor blocked some reaction between isocitrate and the α-ketoglutarate-succinate step in the cycle. The inhibition did not seem to be on the isocitric dehydrogenase, since there was good oxidation of isocitrate in the presence of impure pyruvate or the lactone, although no oxalacetate was formed and no pyruvate was oxidized. A photometric determination of TPN reduction by isocitrate as catalyzed by isocitric dehydrogenase in an acetone powder of rat heart mitochondria (*5*) showed that the lactone had no inhibitory effect in concentrations up to 5 mM.

Essentially complete conversion of 5 mM pyruvate to α-ketoglutarate was obtained when 1 mM lactone was present, and equally good conversion was seen from isocitrate. Since these results would point to a block on the α-ketoglutarate oxidase, we examined the effect of the lactone on this enzyme isolated from pig heart (*6*) by one of us (C.M.M.) with the help of D. R. Sanadi at the Institute for Enzyme Research, Madison. When α-ketoglutarate and the lactone were present in equimolar concentration, inhibition of 50 percent was observed. This inhibition would seem to be competitive, since increasing the concentration of the α-ketoglutarate reduced the inhibition. The oxalacetigenic ability of α-ketoglutarate in the mitochondria was inhibited even more potently than the oxidase preparation. The block in the cycle would, therefore, seem to be due to this competitive inhibition of the α-ketoglutarate oxidase. Blocking of the initiation of pyruvate oxidation by citrate or isocitrate, or of the normally operating cycle, would be much more complete owing to the low concentrations of α-ketoglutarate present under these circumstances.

Titration of the lactone demonstrated two acidic groups with $pK_1 = 2.35$ and $pK_2 = 6.95$. The first dissociation constant refers to the normal free carboxyl group, but pK_2 is too high for a carboxyl group and would argue strongly against the presence of the straight-chain dimer (where pK_2 would be expected to be between 4.5 and 5.0). Cleavage of the lactone ring near neutrality is unlikely, since rapid back titration showed identical values for the pK's and it is doubtful that ring closure would occur rapidly under these conditions. There remained the possibility that enolization takes place and that form III is prevalent around neutrality, the pK_2 referring to the enolic hydroxyl group whose acidic strength is increased by the surrounding groups and chelation with cations. Titration of diethyl-oxalacetate, which possesses a similar —CO—CO—CH_2— grouping showed that the pK of the enolic hydroxyl here was 7.6. Thus we assume that the inhibitor is present in aqueous solution as the lactone and around neutrality in the enolic form (III). Permanganate reduction indicated an active double bond in the prepared lactone at neutrality, again suggesting the enolic form.

Preliminary work on liver and kidney mitochondria demonstrated that the cycle is not blocked so readily by the lactone as in heart mitochondria. We are at present attempting to purify the lactone and related substances, investigating the more intimate mechanism of the inhibition, as well as studying the action of the inhibitor on the functional activity of rat cardiac muscle.

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2 August 1954.

Carbon Dioxide Utilization by Rabbit Liver

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During the investigation of labeled carbon dioxide fixation into the organic acids of liver homogenates, it was observed that such incorporation of the isotope in the liver of the rabbit differed from that of other species examined (*1–5*). Fixation was evident within the times described into a component of the acetone extracts insoluble in the solvent that readily dissolves the organic acids. Unlike any other species examined, the extent of the incorporation into the insoluble compound was as great and at times greater than that into such acids as succinic, fumaric, and malic.

Liver tissue from three adult rabbits was incubated with $NaHC^{14}O_3$ (*6*) under the conditions previously described (*5*). Incubations were for 10 min except where indicated. Acetone extracts were prepared. The chromatography and radioactive assays have been outlined in other experiments (*3, 5*). The paper chromatographic separations were those of Denison and Phares (*7*) and Benson *et al.* (*8*) and the tests for sugars followed the procedures of Dische (*9*).

The data of Table 1 indicate that the fixation of the

Table 1. Distribution of radioactivity within acetone extracts of rabbit liver homogenates incubated with $NaHC^{14}O_3$, 0.47 gm tissue was incubated in 1 ml modified (*5*) Krebs ringer solution containing 0.005 mc of the isotope; cts means "counts," where the counter efficiency is 2 percent.

Solute	Rf*	Time of incubation (min)									
		3		5		10		20		30	
		(cts/min†	%)	(cts/min	%)	(cts/min	%)	(cts/min	%)	(cts/min	%)
Compound insoluble in amyl alcohol-chloroform	0	1562	39.0	1632	38.1	3264	70.6	4224	81.6	5990	77.9
Malic acid	0.38	1907	47.4	2112	49.2	1088	23.5	819	15.8	1427	18.6
Succinic and lactic acids	0.75	544	13.6	544	12.7	275	5.9	134	2.6	275	3.5
Total activity of labeled compounds		4013		4288		4627		5177		7692	

* Ether-acetic acid-water (13-3-1) was the developing solvent for the paper chromatograms.
† Approximately one-twentieth of the total extract of the liver was applied in each case.

label into the amyl alcohol-soluble compound was not limited to an incubation time of 10 min exclusively. The percentages of the total fixation into malate at 3 and 5 min exceeded those at 10, 20, and 30 min. Since the chemical concentration of the malate did not change, these percentages mirror the changes in specific activity. On the other hand, the abundance of the label in the insoluble residue was lower at 3 and 5 min and greater at 30 min. In butanol-acetic acid-water (4-1-5), the insoluble residue moved on paper as a single spot (Rf 0.2), which gave a positive test for phosphate with acid molybdate, benzidine, and sodium acetate (*8*). When the eluted spot from butanol-acetic acid-water was hydrolyzed in HCl and rechromatographed, it was not found to be a hexose or triose. The rechromatographed spot, tested with diphenylamine, showed that difference (*9*) between the optical density D at 660 and 580 mμ ($D_{660} - D_{580} = D_{400}$) that is characteristic of glycolaldehyde. However, the spectral absorption between 500 and 700 mμ was not identical to that of the product from the known glycolaldehyde, even though the mobility of the compound on paper in the butanol-acetic acid-water system was like that of the authentic glycolaldehyde.

Such relative incorporation into the organic acids and the insoluble compound at the several times of incubation shown here distinguishes carbon dioxide fixation in the liver of the rabbit from similar findings in other species. If the utilization of the label by the organic acids and the compound insoluble in amyl alcohol-chloroform occurs by independent mechanisms and if the insoluble compound is glycolaldehyde phosphate, the data could be explained by current views concerning the path of carbon in animal cells (*10*). By such views it would be presumed that the carbon was first fixed into a hexose, the precursor of sedoheptulose which later cleaved between carbons 2-and 3 to produce the labeled glycolaldehyde.

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Activity in Electrogenic Organs of Knifefishes

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The knifefishes, which comprise the family Gymnotidae, and inhabit fresh tropical waters of Central and South America, are close relatives of the electric eel, *Electrophorus electricus*. They possess structures that resemble the electric organ of the eel, but identification of these with functional electric organs has been doubted (*1*). Only a single report (*2*) mentions electric activity in *Gymnotus carapo*.

Three species of knifefishes examined in a preliminary survey in this laboratory have all proved to be electrogenic. These are *Eigenmannia virescens*, *Gymnorhamphichthys hypostomus*, and *G. carapo*. Unlike the eel, which emits single or short bursts of pulses of high intensity, up to 600 v and 1 amp, these fish emit low intensity pulses (Fig. 1) continuously and with remarkable regularity (Fig. 2). In this they resemble the Mormyridae of Africa, *Gymnarchus* (*2*), *Mormyrops boulengeri* (*2*), and *Mormyrus kannume* (*3*).

The responses were recorded from intact fishes swimming freely or lying on the inclined floor of a tank with only the head immersed. The electrodes were wires, spaced 5 mm to several centimeters apart, insulated except at their tips, and placed near the swim-

ming fish or alongside the quiescent ones. Despite shunting by the water, the responses, recorded oscillographically, were 10 to 300 mv in amplitude. The magnitudes preclude the possibility that the activity derives from muscles, since only electric organs are known to have in their cells the specific adaptation that permits series addition of the emf's generated by the responses of the individual cells (*4, 5*).

At 27°C the fish emitted discharges at rates of 300 (*E. virescens*), 100 (*G. hypostomus*) or 65 per second (*G. carapo*). The variations in frequency from time to time were only 10 to 20 percent. When the entire fish, or only its head was cooled, the frequency of the discharges decreased (Fig. 2). In all three species the change with temperature had a Q_{10} of 1.5 (Fig. 3).

The decrease in frequency produced by cooling only the head indicates that the discharges are centrally controlled, probably by the brain. The identical Q_{10} for all three species indicates that the control mechanism is probably the same in all. The forms of the discharges, shown in Figs. 1 and 2, and their changes with temperature cannot be evaluated from these experiments. The activity was recorded from intact fish, 10 to 30 cm long, having different geometries of electric organs, with different electrode spacings and various orientations of the fish toward the electrodes.

The significance to their economy of the rhythmically pulsatile discharges continuously emitted by the Mormyridae and knifefishes is unknown. When quiescent, the eel produces no detectable electric activity. It has been reported (*6, 7*) that when cruising in large tanks eels emit low voltage discharges at about 50 per second. The suggestion has been made (*6*) that these discharges serve to orient the fish with regard to obstacles. Were the rhythmic electric activity of knifefishes and Mormyridae to subserve this function, highly specialized, as yet unknown, sense organs might be required. The recognition of distortions, caused by solid

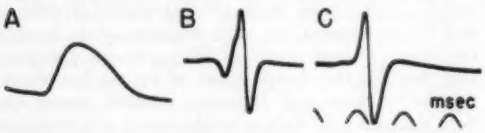

Fig. 1. Individual pulses from the series continuously emitted by three species of knifefishes. The forms changed with orientation of the fish to the electrodes and with electrode spacings. The amplitudes also depended on the geometry of the recording conditions. (*A*) *E. virescens*, (*B*) *G. carapo*, (*C*) *G. hypostomus*. Time in milliseconds.

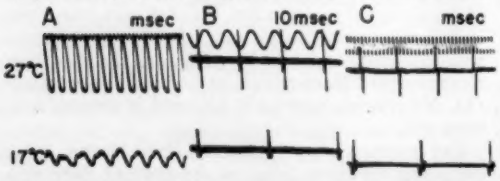

Fig. 2. Dependence of the frequency of the discharges on temperature. *A*, *B*, *C*, as in Fig. 1. Only the head of *G. hypostomus* (*C*) was cooled in this experiment.

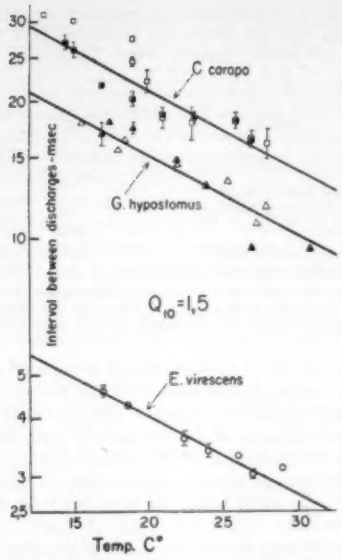

Fig. 3. Temperature coefficients of the discharges. Filled symbols represent duplicate experiments. The extent of variations in frequency is shown by the lines though averaged values.

objects, of the potential field produced in the water by the discharges would demand extremely sensitive, highly differential electric detectors.

The cells of the electric organs of the knifefishes, in their structure and organization, appear to resemble those of the organs in the electric eel (*8*). Recent studies of unitary activity in the latter (*4, 5, 9, 10*) and in *Raia clavata* (*11*) have disclosed important features belonging to the general properties of bioelectric generators as well as special adaptations that make for electric organs. The existence of electrogenic properties in all three knifefishes examined in this survey indicates that others of the approximately 50 species in this family might also possess these. Some are relatively easily obtainable tropical fishes. This offers additional material for investigations on electric organs as well as the possibility for further insight into problems of bioelectric activity.

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1 July 1954.

Inhibition of Influenza and Mumps Virus Multiplication by 4,5,6- (or 5,6,7-) Trichloro-1-β-D-Ribofuranosyl-benzimidazole

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Results reported earlier (*1*) indicated that the marked influenza virus inhibitory activity of 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole (DRB) was related to (i) the presence of the ribofuranose moiety at position 1, and (ii) the presence of unnatural (Cl) substituents in the benzenoid ring, two such substituents showing a more marked effect than one. It appeared that further increase in activity might be achieved by additional substitution in the benzenoid ring while retaining the ribofuranosyl group at position 1.

4,5,6- (or 5,6,7-) Trichloro-1-β-D-ribofuranosylbenzimidazole (TRB; see Fig. 1) (*2*) was synthesized (*3*) and tested for its inhibitory action on Lee-virus multiplication in chorioallantoic membranes *in vitro* in a manner described previously (*1, 4*). The inhibitory activity of TRB was compared with that of other derivatives in terms of the molar concentration that caused 75-percent inhibition of multiplication. For the purposes of this study, unsubstituted benzimidazole was considered as the reference compound. This substance causes 75-percent inhibition at a concentration of 0.0035*M* or 410 μg/ml and has been assigned a relative inhibitory activity of 1 (*1, 4*). It was found that TRB caused this degree of inhibition of Lee-virus multiplication at a concentration of 0.0000046*M* or 1.6 μg/ml. As can be seen in Table 1, under identical conditions 0.000038*M* or 12 μg/ml of DRB is required to produce the same effect (*1*). On a molar basis, the trichloro compound has 8 times greater activity than the dichloro derivative. It should be emphasized that TRB is 760 times more active, whereas DRB is 92 times more active, than unsubstituted benzimidazole. In Table 1 attention is also directed to the structure-activity relationships (*1*) that establish the importance of the ribofuranose moiety.

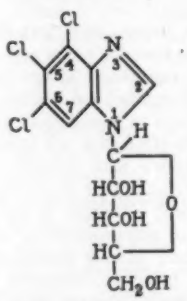

Fig. 1. 4,5,6- (or 5,6,7-) Trichloro-1-β-D-ribofuranosyl-benzimidazole (TRB).

The medium used in these experiments consisted of a buffered salt and sugar solution containing Na_2HPO_4, KH_2PO_4, NaCl, $CaCl_2$, $MgCl_2 \cdot 6H_2O$, and dextrose. In order to determine whether, in the presence of a more complex medium, the degree of inhibition would be similar, a medium (*5*) that included bicarbonate, vitamins, amino acids, and purine and pyrimidine bases was employed in separate experiments. Before incubation was started, the *p*H of the complex medium was adjusted to 7.2 by passing a mixture of CO_2 and O_2 through culture tubes. It was found that the yield of virus at 46 hr in the absence of TRB was no greater in the complex than in the control medium. In the presence of TRB (0.0000065*M*) the degree of inhibition was similar (90 percent) in the two mediums.

Previous attempts to block the inhibitory action of DRB with selected compounds that might serve as metabolites were unsuccessful (*1*). Attempts were made to block the inhibitory action of TRB with a mixture of adenosine (0.001*M*), vitamin B_{12} (25

Table 1. Activities of benzimidazole derivatives as inhibitors of influenza-B virus (Lee) multiplication in the chorioallantoic membrane *in vitro*.*

Benzimidazole derivative	Inhibitory concentration (*M*)†	Inhibitory activity relative to benzimidazole
Benzimidazole‡	0.0035	1.0
5- (or 6-) Chloro-1-β-D-ribofuranosyl	.00028	13
4,6- (or 5,7-) Dichloro-1-β-D-ribofuranosyl	.00010	35
5,6-Dichloro-1-β-D-ribofuranosyl (DRB)	.000038	92
4,5,6- (or 5,6,7-) Trichloro-1-β-D-ribofuranosyl (TRB)	.0000046	760
5,6-Dichloro-1-β-D-ribopyranosyl	.00023	15
5,6-Dichloro-1-β-D-arabinopyranosyl	.0011	3.1
5,6-Dichloro-1-β-D-glucopyranosyl	.0011	3.1

* Each culture consisted of 6.6 cm^2 of chorioallantoic membrane suspended in 1 ml of medium. Inoculum: Lee virus, $10^{6.1}$ EID_{50}. Six cultures were used per group and several groups were employed with various concentrations of each compound. Cultures were incubated at 35°C for 36 hr with shaking. Virus was measured by the hemagglutination technique in the medium (*1, 4*).

† Concentration giving 75 percent inhibition of multiplication.

‡ Considered as the reference compound.

μg/ml), folic acid (0.00017*M*), and coenzyme 1 (0.0001*M*). It was found that such supplementation of the simpler medium did not result in increased virus production by the chorioallantoic membrane. Furthermore, no significant blocking of the inhibitory action of 0.0000065*M* TRB by the supplements used was noted.

Previous studies (*1*) showed that DRB is capable of inhibiting Lee-virus multiplication in embryonated eggs and in mice without causing significant signs of toxicity in either host. In view of these results and the results described here, extension of the animal studies to other viruses appeared indicated. The effect of DRB and of TRB on the multiplication of mumps virus in 8-day-old embryonated eggs was determined. As can be seen in Table 2, both compounds caused marked inhibition of multiplication of mumps virus in the allantoic sac of embryonated eggs. Precise quantitative comparison of the effects of DRB and TRB *in vivo* is vitiated by the low solubility of these compounds. In the *in vivo* experiments, both DRB and TRB were used in suspension form. Under the experimental conditions employed, neither compound caused obvious slackening of the spontaneous activity of the embryos. No deaths attributable to DRB or TRB occurred.

The results reported here lend further support to the contention (*1*) that an unnatural benzimidazole nucleus, particularly with respect to the benzenoid ring, is of great importance in relation to the virus-inhibitory activity of the ribofuranosides of benzimidazole. Previous observations (*1, 3*) that the inhibitory activity cannot be blocked by certain suspected metabolites have been extended. The finding that DRB and TRB inhibit mumps-virus multiplication *in vivo* without causing apparent damage to the host indicates that these compounds are selective in their action. However, it is doubtful (*1, 6*) that these compounds interfere with chemical reactions that are specific for the viruses and do not occur in the uninfected host. It appears that the explanation for the selective action may concern the relative quantitative importance of certain metabolic processes for the virus as compared with the host and intracellular factors of accessibility.

Table 2. Inhibition of mumps-virus multiplication by benzimidazole derivatives *in ovo*.*

Compound	Incubation (hr)	Hemagglutination titer† of allantoic fluid
None	96	128
DRB	96	< 2
TRB	96	< 2
None	120	512
DRB	120	16
TRB	120	22

* Inoculum: mumps virus, $10^{8.9}$ EID_{50}. Thirty minutes after inoculation of virus each egg received, by allantoic injection, 0.25 ml of saline, or compound suspended in saline. One milligram of either DRB or TRB was injected per egg.

† Expressed as the reciprocal of dilution at end-point. Six eggs were used per group, and aliquots of infected allantoic fluid were pooled for titration. Final concentration of chicken RBC was 0.045 percent.

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27 July 1954.

On the Nonidentity of Bence-Jones Proteins

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A century ago Bence-Jones first described urinary proteins that now bear his name and are identified by the property of coagulation at low temperature (45° to 55°C) with dissolution on boiling. These proteins occur rarely, always in association with some pathology and are most often, but not invariably, found in the urine of patients with multiple myeloma. Some workers have concluded that Bence-Jones proteins are chemically identical, although it has been shown by immunological and physicochemical analysis that different patients may exerete biologically and molecularly dissimilar proteins. Recently, in a study of Bence-Jones proteins obtained from nine cases none were found to be identical in all the physical properties studied—that is, sedimentation constant (s_{20}), diffusion constant, isoelectric point *pI*, *p*H-mobility curve, and stability in dilute acid or alkali (*1*).

In further characterization of normal plasma proteins and of the pathological proteins in multiple myeloma by means of N-terminal amino acid analysis, Bence-Jones proteins from eight cases have thus far been studied. The fluorodinitrobenzene method of Sanger (*2*) was used to detect and estimate the N-terminal amino acids (that is, terminal residues having a free amino group). Buffered silica gel or celite was employed for chromatographic separation of the dinitrophenyl (DNP) derivatives, and paper chromatography for their identification (*3–5*). As is shown in Table 1, six of the eight proteins were similar in s_{20} (about 3.3 Svedberg units) but were distinguishable by their electrophoretic properties. Proteins B, E, and G migrated electrophoretically with skewed patterns indicative of heterogeneity but unlike Ma did not separate into two components within the *p*H stability range (*p*H 5 to *p*H 9). A, D, F, and Ag con-

Table 1. N-terminal groups of Bence-Jones proteins.*

Protein	s_{20}	Mobility (*p*H 8.6)	*pI*	Aspartic acid	Glutamic acid	Serine	Threonine	Leucine	Tyrosine
				(moles per 44,000 g)					
A	3.41	−4.7	4.75	1.50	0.07	0.12	0.05		
F	3.08	−3.4	4.9	1.62	0.13	0.08	0.05		
Ag	2.14	−2.2		1.71					
Ma	2.25	−4.0		1.17	0.07	0.03	0.16		
B	3.14	−4.2	4.6	trace	trace	0.52			
D	3.44	−2.4	5.5	0.06	0.04	0.04			
E	3.36	−1.4	6.7	< 0.01		0.05			
G	3.28	−2.6	5.6					0.12	> 0.74

* s_{20} (in Svedberg units) and mobility (in units of 10^{-5} cm^2 sec^{-1} v^{-1}) were determined in *p*H 8.6 veronal buffer, 0.1 ionic strength (*1*). Calculations assume literature values for hydrolytic destruction of DNP-amino acids and a protein content of 75 percent for the DNP-protein. For further physical data on A, B, D, E, F and G, see (*1*).

tained about 3 percent of a faster moving component upon electrophoresis at *p*H 8.6.

Of the eight proteins, four had essentially only aspartic acid in the N-terminal position, whereas this amino acid was either undetected as an end-group or present as such only in trace amounts in the other proteins. The latter, in fact, fell into three types according to the nature of their amino end-groups. The N-terminal amino acid content per 44,000 g (the molecular weight of A, D, and proteins of similar s_{20}) was as follows: A, F, Ag, and Ma, 1.2 to 1.7 moles of aspartic acid; B, 0.5 mole serine; G, about 1 mole of tyrosine plus some leucine(or isoleucine). In several attempts only traces of ether-soluble DNP-amino acids were obtained from E, a crystalline protein having the highest *pI* or from D with a *pI* of 5.5. Integral values are to be expected for a chemically homogeneous protein that does not have a cyclic structure. Fractional values for the minor end-groups indicate chemical heterogeneity. Protein B, which contained a nonstoichiometric amount of N-terminal serine, was physicochemically the most heterogeneous protein. No correlation has yet appeared between the nature of the end-group and physical properties such as *pI* or s_{20}, with electrophoretic patterns of the serum or with hematological or clinical findings.

Thus, although the eight subjects each excreted predominantly only one type of Bence-Jones protein, there were at least four kinds on the basis of the N-terminal amino acid, two groups from s_{20}, three from the isoelectric point, and up to five according to mobility. Differences in the amino acid composition of Bence-Jones proteins probably exist, but reliable analyses of physically homogeneous specimens from different patients have not yet been reported. Hence, this is the first evidence that Bence-Jones proteins excreted by various individuals differ in chemical structure as well as in physical constants. Similar differences in end-groups have been reported for the pathological globulins of multiple myeloma serums (*6*). Isotopic investigation, however, has yielded evidence that the Bence-Jones proteins are not derived by degradation of serum or tissue proteins (*7*), and the origin and function of these unique urinary proteins remain unknown.

Note added in proof. Since the submission of this manuscript, G. Biserte of the Laboratoire de Chimie Biologique, University of Lille, France, has informed us of work now in progress in collaboration with P. Burtin of the Institut Pasteur, Paris. Of four cases of Bence-Jones proteins investigated by these workers, three contained N-terminal aspartic acid, and one was devoid of ether-soluble DNP-amino acids. We, ourselves, have recently studied a crystalline Bence-Jones protein that differed in N-terminal groups from all those listed in Table 1.

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29 July 1954.

Blood Serum Protein of the Marine Elasmobranchii

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Species differences of serum protein fractions have been shown electrophoretically by Deutsch and Goodloe (*1*), Deutsch and McShan (*2*), Moore (*3*), Gleason and Friedberg (*4*), and Janssen (*5*). Janssen claimed that although the relative amount of serum components may vary considerably, all components (albumin, α-, β-, γ-globulin) are present in each animal; thus, he concluded that all animals have a common plan of producing serum protein. But the afore-mentioned experimenters did not study the serum pattern of the Elasmobranchii.

In our experiments we gathered data on the blood serum protein of the skate, *Raja kenojéi* Müller et Henle, and the shark, *Heterodontus japonicus* Duméril.

Blood samples were obtained directly from the aorta. Japanese hand-worked paper and Whatman filter paper No. 1 (*6*) were used for the carrier of the protein. Compared with the latter, the former is very thin, but its fibers are almost parallel and its strength was sufficient for our purpose (*7*). A rectified 220-v with a current of 0.5 ma was used throughout the experiment; M/20 veronal-buffer solution was adjusted to *p*H 8.6. The paper was stained with 1-percent bromphenol blue (B.P.B.) solution containing $HgCl_2$, as previously described (*8*).

The relative mobility of the fastest component of these Elasmobranchii serums was not electrophoretically the same as that of other animals. Figure 1 shows the comparison of the pattern of shark serum and that of human serum. Both serums were run parallel in the same apparatus at the same time.

From these data, it appears that the Elasmobranchii serum does not contain albumin fraction. In another experiment, we used a shark serum that was mixed with horse serum albumin (Fig. 2). It is interesting to note that in the mixture, the horse serum albumin moves faster than any other components of the shark serum.

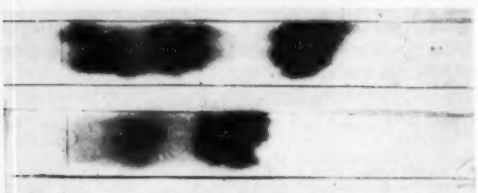

Fig. 1. (Top) Human serum; (bottom) shark serum, showing lack of albumin component.

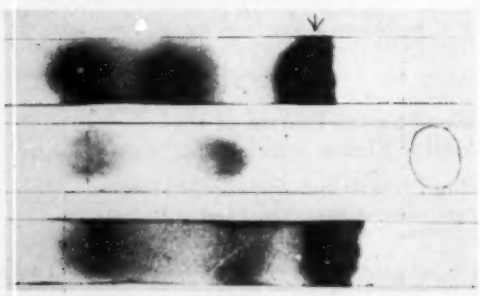

Fig. 2. (Top) Human serum; (middle) shark serum; (bottom) shark serum plus horse serum albumin, showing that the fastest component of shark serum differs from mobility of albumin. Arrow or circle shows the place that B.P.B. moved. In the top paper B.P.B. moved with the fastest component (albumin), but in the middle paper B.P.B. moved independently with the shark serum. In the bottom paper B.P.B. moved with the horse serum albumin. These papers indicate lack of albumin component in shark serum.

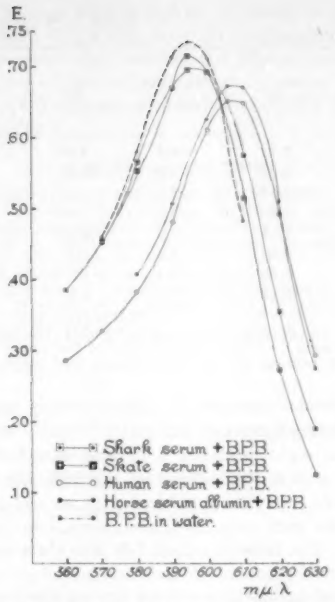

Fig. 3. Optical density of B.P.B. solution in serums of shark and skate, compared with that in human serum and horse serum albumin. Abscissa is the wavelength; ordinate is optical density. In each case, 0.1 ml of 0.05 percent B.P.B. was added to 2.0 ml of M/15 phosphate buffer (*p*H 7.2) and 0.2 ml of serum was used.

For another proof of this fact, 0.05-percent B.P.B. solution was added to each serum in the experiment. Usually, B.P.B. moves with horse serum albumin, but in the shark serum B.P.B. moved independently from the serum fraction (Fig. 2). From this observation it seems that the fastest component of the shark serum is different from horse serum albumin, since the dye combines with native albumin (*9*).

This difference of dye combination was also demonstrated spectrophotometrically (Beckman, Type DU). Bromphenol blue has an absorption maximum at 595 mu, but when it was combined with albumin the absorption maximum changed to 605 mu for its metachromasia (Fig. 3). When Elasmobranchii serums were added, it stopped at 595 mu. That is, these serums do not show metachromasia.

These facts suggest that the fastest component of Elasmobranchii serum differs from that of other animal serums and suggest that the lower vertebrates do not have the same plan of producing serum protein as do the higher vertebrates.

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24 May 1954.

Glucose-6-Phosphatase Studies in Fasting

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Glucose-6-phosphatase, an enzyme, which hydrolyzes glucose-6-phosphate to glucose and inorganic phosphate, was first demonstrated by Fantl *et al.* (*1*) and has been studied by Swanson (*2*) and De Duve *et al.* (*3*). The enzyme has been demonstrated in different organs, but it is the most active in liver and kidney. It can be distinguished from other nonspecific phosphatases by its *p*H optimum (6.5 to 6.8), its thermal instability, its sensitivity to acids, and its substrate specificity on glucose-6-phosphate, with negligible or no activity toward glycerophosphate, glucose-1-phosphate, or fructose-6-phosphate. The liver enzyme is associated mainly with the microsome fraction. Chiquoine (*4*) demonstrated with histochemical method that the enzyme is more abundant in the peripheral third of the hepatic lobule than in the inner two-thirds. Within the hepatic cell glucose-6-phosphatase is concentrated about the nuclear membrane.

However, there is very little known about the physiological and pathological behavior of this enzyme. Cori and Cori (*5*) demonstrated its importance in the pathology of carbohydrate metabolism. They reported the almost complete absence of the enzyme from liver in human cases of glycogen storage disease.

A well-established fact is that liver is virtually the sole source of the blood sugar in the fasting animal (*6*). Since the blood sugar level is maintained throughout long periods of fasting, the glucose secreted by the liver into the blood, therefore, must be derived from stored carbohydrate or noncarbohydrate precursors. It seemed to be of interest to study the behavior of liver glucose-6-phosphatase in fasting (*7*).

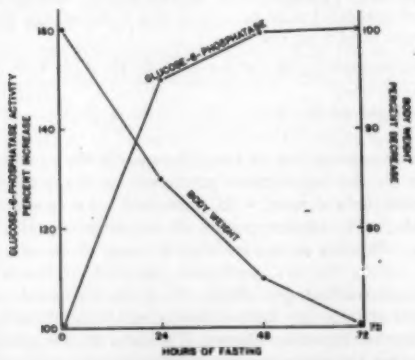

Fig. 1. Effect of fasting on body weight and liver glucose-6-phosphatase activity in mice.

Table 1. Effect of 48-hr fasting on the glucose-6-phosphatase activity in rat liver.

Rat	Body weight (g)	Liver glycogen (g percent)	Liver glucose-6-phosphatase activity*
Controls: fed chow			
1	210	4.80	292
2	210	4.96	292
3	210	2.91	185
4	210	4.26	321
5	210	3.00	250
6	210	4.20	281
Mean	210	4.02	270
Percentage	100	100	100
Fasted: for 48 hr			
7	180	0.12	415
8	185	.06	467
9	190	.09	395
10	190	.09	421
11	178	.01	410
12	180	.32	381
Mean	184	0.22	432
Percentage of control values	88	5.5	160

* Expressed in micrograms of phosphorus liberated in 15 min at 31°C per 100 mg liver wet weight.

Twenty-eight male albino mice (31 to 33 g) were divided into four groups, each containing seven mice. The three fasting groups received no Purina Fox Chow for 24, 48, and 72 hr. Water was given *ad libitum* to all groups. Animals were sacrificed by a blow on the head, decapitated, and bled. Livers were quickly excised and pooled on ice and 5-percent homogenate was prepared in 0.25*M* sucrose. The glucose-6-phosphatase was assayed according to the method of Cori and Cori (*5*). Incubation time was 30 min at 31°C. Figure 1 shows the increase in glucose-6-phosphatase activity as expressed in percentage increase when the control value is taken as 100 percent.

The increased liver glucose-6-phosphatase activity was also demonstrated in fasting rats. The following experiment is a representative example. Twelve male Wistar rats of weight 210 g were separated into two groups. The control group had a free access to Purina Fox Chow and water, while the fasting group received only water for 48 hr. Animals were sacrificed, and the enzyme was determined as described in the foregoing paragraph, except that 10-percent homogenates were prepared from each liver, and they were assayed in separated, instead of pooled, livers. Incubation time

was 15 min at 31°C. A small sample of tissue was rapidly snipped from the right lobe of the liver for glycogen estimation. This was determined by the method of Good, Kramer, and Somogyi (*8*), employing the Nelson's adaptation of the Somogyi method for glucose (*9*).

Table 1 shows that while the rats lose about 12 percent of body weight during the 48-hr fast and liver glycogen decreases to 5 percent of the original value, the glucose-6-phosphatase activity is increased by 60 percent.

These experimental data have been repeatedly confirmed in this laboratory in the course of other experiments involving various periods of fasting, and it was found that the difference between the glucose-6-phosphatase activity of normal and 48-hr fasted animals is significant also when expressed on nitrogen or liver weight-to-body weight ratio basis (*10*).

The afore-cited data demonstrate that the glucose-6-phosphatase activity increases in the liver of fasting mice and rats. A survey of the literature on the effect of fasting on liver enzymes shows that most enzymes decrease under the described conditions here. The increase of glucose-6-phosphatase activity during fasting can, therefore, be considered as a physiological adaptive change to the stress of fasting during which the glycogen stores of the liver are depleted.

References and Notes

* Senior fellow, Cancer Research Society, Montreal.

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2. M. J. Swanson, *J. Biol. Chem.* **184**, 647 (1950).
3. C. De Duve *et al.*, *Bull. soc. chim. biol.* **31**, 1242 (1949); H. G. Hers and C. De Duve, *ibid* **32**, 20 (1950); H. G. Hers *et al.*, *ibid.* **33**, 21 (1951).
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7. This project has been supported by grants from the Cancer Research Society. The valuable assistance of Vilma Jansons is gratefully acknowledged.

8. C. A. Good, H. Kramer, and M. Somogyi, *J. Biol. Chem.* **100**, 485 (1953).
9. N. Nelson, *ibid.* **153**, 375 (1944).
10. Unpublished.

6 July 1954.

Communications

Inherited Jaundice in *Peromyscus*

This is to report (*1*) a mutation in *Peromyscus maniculatus* (*2*) that is typically associated with neonatal jaundice, chronic splenomegaly, anisocytosis, polychromatophilia, and reticulocytosis. Affected mice usually become jaundiced during their first postnatal 24 hr. The duration of the yellow color varies but it is not, as a rule, perceptible after the second postnatal day. The intensity of the color varies from deep to pale yellow, and in some individuals it may not be sufficiently marked to make identification possible upon first inspection.

The yellow color is succeeded by pallor, which may be very pronounced and may last until the fifth postnatal day when, in any event, it would be masked by the outgrowing pelage. All of more than 50 jaundiced young that were examined on successive days became pallid if they survived, and this symptom, because of its duration, is more useful than the neonatal jaundice in the identification of affected individuals.

All of 30 newborn mice recorded as jaundiced and/or pale had splenomegaly when, to test the point, they were posted at 3 mo of age or later. A much larger number of mice examined at an age when affected individuals would be jaundiced or pale, and recorded as not affected, had spleens of normal color and proportions. The normal spleen in the deer mouse is a slender leaflike organ that is pale red or dark red in color. Jaundiced mice develop a spleen that is very dark red or black in color and about double the size of the normal spleen in each dimension. There is variation in the size and color of both normal and hypertrophied spleens, but intergradation in size or color has not yet been observed.

The erythrocytes of adult splenomegalic mice vary in size and shape and this erythrocytic variability is an immediately obvious feature upon microscopic examination of either blood smears or the vascular areas of tissue sections. Blood smears of affected mice, stained by the Osgood-Wilhelm technique (*3*), have, in the 22 cases examined, exhibited a significantly higher proportion of reticulocytes than was found in the blood of normal individuals, of similar age, prepared at the same time. The reticulocyte counts (*4*) are shown in Table 1.

Table 1. Percentages of reticulocytes in smears made from jaundiced mice between 3 and 6 mo of age and of normal mice 3 mo old.

Percentage	20	18	16	14	12	10	8	6	4	2	n
Normal mice										7	7
Jaundiced mice	2		1		6	3	2	1			15

A chi-square test of the difference in the number of mice in the two classes produced by the mating of normal hybrid mice with jaundiced mice is given in Table 2. The phenotypes of all parent mice and all of their offspring were identified by more than one person during the first postnatal day and, if necessary, on a succeeding day. Since 15 of the 19 broods contained young of both classes, comparison assisted separation into two classes. The data fit the assumption that the characteristics of the syndrome described here are brought about by a single recessive gene effect.

Table 2. Number of young in the two classes produced by mating jaundiced mice with nonaffected hybrids. Expected ratio 1:1. P based on one degree of freedom.

Class	Observed	Expected	Chi-square	P
Jaundiced and/or pale	38	39		
Not jaundiced	40	39	0.52	.95–.70

In addition to the data here tabulated we have a larger number of young produced by test crossing females, identified as probable hybrids by pedigree inspection and progeny test, with jaundiced males. These test crosses have produced 70 normal and 63 jaundiced or pale mice. Jaundiced mice, mated *inter se*, have produced 27 jaundiced or pale mice and two that were cachectic but without the typical jaundice or pallor.

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RUTH ANDERSON

University of Oregon, Eugene

References and Notes

1. This research was assisted by a grant from the University of Oregon Graduate School.
2. F. B. Sumner, *Am. Naturalist* **49**, 688 (1915); L. R. Dice, *Am. Naturalist* **74**, 289 (1940).
3. E. E. Osgood and M. M. Wilhelm, *J. Lab. Clin. Med.* **19**, 1129 (1933-34).
4. The reticulocyte counts were made through the kindness of Osgood and Koler at the University of Oregon Medical School.

25 October 1954.

New Etiologic Agent in Nonspecific Bacterial Vaginitis

This is a preliminary report of an investigation in progress dealing with the etiology and clinical manifestations of "nonspecific" bacterial vaginitis. The etiology of the condition has previously been ascribed to a large group of unrelated bacteria. An intensive search of the literature has not revealed evidence that a regularly appearing etiologic agent has been previously found to explain these infections. We have isolated a new bacterium that appears to be the causative agent in the vast majority of so-called "nonspecific" vaginitides.

The investigation includes a clinical and bacteriological study of 91 cases of bacterial vaginitis. A previously unidentified and unclassified organism belonging to the genus *Haemophilus* has been isolated in 81 of the 91 cases. Although the organism was predominant in each of the 81 cases from which it was isolated, it occurred in pure culture on one or more occasions in 62 of the 81 cases.

A compilation of the clinical signs and symptoms suggests that the infection resulting from this organism constitutes a specific disease entity. The discharge is usually gray in color, thin and homogeneous, odorous, and less acid than the secretions of a normal vagina. Itching and irritation, although occasionally present, are not prominent symptoms. The infection has been established in normal (volunteer clinic) patients by direct inoculation of material from the vaginas of infected patients and by material from pure culture.

The organism has been found to be sensitive to the tetracycline group of antibiotics and to sulfonamides. These drugs have been administered orally and intravaginally with the infection being eradicated in the majority of cases.

Although it is felt that a diagnosis usually can be made by correlating clinical manifestations with microscopic findings, cultural methods are necessary for final proof of the infection. Stained smears of the discharge reveal tremendous numbers of small, pleomorphic, gram-negative bacilli. This new organism is extremely fastidious, and isolation has been achieved routinely only on proteose-peptone No. 3 agar containing 10 percent defibrinated sheep blood, incubated under increased carbon dioxide tension (candle jar). The cultural characteristics undoubtedly explain why the organism has escaped previous isolation and identification. A complete report [*Am. J. Obstet. Gynecol.*, in press] describes in detail the isolation and identification of the organism, the clinical manifestations of the entity, evidence of pathogenicity, and so forth. We feel that sufficient evidence is at hand to establish proof of a newly defined specific bacterial vaginitis, the etiology of which heretofore has not been recognized.

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10 October 1954.

Absence of Circulating Antibodies in Patients with Pulmonary Tuberculosis

Serodiagnostic tests of both the complement fixation and hemagglutination type have failed to detect circulating antibodies in a substantial number of patients with active tuberculosis. In recent studies evaluating the hemagglutination test (*1*) the number of negative reactors varied from 14 (*2*) to 44 percent (*3*). This is remarkable in view of the nearly 100-percent incidence of antibody formation in other granulomatous diseases, for instance, coccidioidomycosis or brucellosis.

Under the assumption that substances inhibiting antibody activity may be present, tuberculous serums were fractionated by the cold ethanol method (*4*), which does not accomplish complete separation of the various proteins. The fractions were then tested by both the hemagglutination and complement-fixation methods (*5*). The following results are available. The globulin fractions of three tuberculous serums (No. 1–3), like the whole serums from which they were derived, exhibited activity in both tests. Six serums (No. 4–9, Table 1), apparently devoid of hemagglu-

Table 1. Serologic results on tuberculous serums and their fractions. Fractions are labeled according to Nichols and Deutsch (*4*).

Serum No.	Serum fraction	Titer of: Hemagglutination test	Titer of: Complement-fixation test
4	Whole serum	Neg.	Neg.
	Sup. A	Neg.	Neg.
	Ppt. B	Neg.	Neg.
	Ppt. C_2	Neg.	1: 32
5	Whole serum	Neg.	Neg.
	Sup. A	Neg.	Neg.
	Ppt. B	Neg.	Neg.
	Ppt. C_2	Neg.	1: 256
6	Whole serum	Neg.	Neg.
	Sup. A	Neg.	Neg.
	Ppt. B	Neg.	1: 2
	Ppt. C_2	Neg.	1: 16
7	Whole serum	Neg.	Neg.
	Sup. A	Neg.	Neg.
	Ppt. B	1: 8	1: 1
	Ppt. C_2	Neg.	1: 16
8	Whole serum	Neg.	Neg.
	Sup. A	Neg.	Neg.
	Ppt. B	Neg.	Anticompl.
	Ppt. C_2	1: 8	1: 8
9	Whole serum	Neg.	Neg.
	Sup. A	1: 64	Neg.
	Ppt. B	Neg.	Anticompl.
	Ppt. C_2	Neg.	1: 8
10	Whole serum	1: 20	Neg.
	Sup. A	1: 8	Neg.
	Ppt. B	1: 8	Anticompl.
	Ppt. C_2	1: 16	1: 8
11	Whole serum	Neg.	1: 16
	Sup. A	1: 4	Neg.
	Ppt. B	1: 16	1: 2
	Ppt. C_2	1: 8	1: 16

tinating and complement-fixing antibodies, yielded fractions that gave a positive complement-fixation test. Fractions of three of these serums (No. 7–9) reacted also in the hemagglutination test. Further, fractionation of two tuberculous serums (No. 10 and 11, Table 1) giving a positive reaction in one or the other test furnished proteins manifesting antibody activity of the type seemingly absent in the whole serum.

As a control, five nontuberculous serums were subjected to the same procedures. None of their fractions exhibited antibody activity in the tests mentioned.

These results demonstrate that the absence of antibodies in the tuberculous serums investigated (*6*) was only an apparent one and that fractionation of the serum proteins unmasked antibody activity. The problem whether a substance suppressing antibody was present in these serums or whether fractionation accomplished dissociation of an antibody-antigen complex is under investigation.

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References and Notes

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2. W. Hentel and G. D. Guilbert, *J. Lab. Clin. Med.* **39**, 426 (1952).
3. W. H. Hall and R. E. Manion, *J. Clin. Invest.* **30**, 1542 (1951).
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6. This investigation was supported by grants from the Committee on Medical Research of the American Trudeau Society, Medical Section of the National Tuberculosis Association, and from the California Tuberculosis and Health Association.

28 September 1954.

Availability of Crystalline DL-α-Lipoic Acid

Studies conducted in this and other laboratories during the past decade have culminated recently in the isolation of an extremely active biocatalyst that has been designated α-lipoic acid (*1*) and Protogen-A (*2*). This substance is a growth factor for several microorganisms and has been shown to participate in the oxidative decarboxylation of pyruvic and α-ketoglutaric acids.

Although α-lipoic acid has been identified and obtained synthetically in racemic form (*3–5*), it is not generally available for biological research. In the belief that the nutritional and therapeutic value of this biocatalyst will be assessed only when it is made readily available to interested investigators, we have devoted our time recently to developing an improved synthesis of DL-α-lipoic acid. As a result we have on hand a significant quantity of the crystalline substance which we wish to make available to those interested in exploring its potentialities. Requests for samples should be sent to the address given below.

Lester J. Reed
Biochemical Institute, University of Texas, Austin 12

References and Notes

1. L. J. Reed *et al.*, *J. Am. Chem. Soc.* **75**, 1267 (1953).
2. E. L. Patterson *et al.*, *ibid.* **76**, 1823 (1954).
3. C. S. Hornberger, Jr., *et al.*, *ibid.* **75**, 1273 (1953).
4. M. W. Bullock *et al.*, *ibid.* **76**, 1828 (1954).
5. The racemic form is designated DL-α-lipoic acid (*3*) and 6-thioctic acid (*4*).

13 October 1954.

Meetings & Conferences

December

26–28. American Statistical Assoc., Berkeley, Calif. (S. Weiss, 1108 16 St., NW, Washington 6.)

26–29. National Science Teachers Assoc., Berkeley, Calif. (R. H. Carleton, 1201 16 St., NW, Washington 6.)

26–30. Inst. of Mathematical Statistics, Berkeley, Calif. (K. J. Arnold, Dept. of Mathematics, Michigan State College, E. Lansing.)

26–31. AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, annual, Berkeley, Calif. (R. L. Taylor, 1515 Massachusetts Ave., NW, Washington 5.)

26–31. American Nature Study Soc., Berkeley, Calif. (H. B. Ross, State Teachers College, Fitchburg, Mass.)

27. Metric Assoc., Washington, D.C. (V. G. Shinkle, 1916 Eye St., NW, Washington 6.)

27–28. American Folklore Soc., New York, N.Y. (M. Leach, Bennett Hall, Univ. of Pennsylvania, Philadelphia 4.)

27–28. Ecological Soc. of America, Berkeley, Calif. (J. F. Reed, Dept. of Botany, Univ. of Wyoming, Laramie.)

27–29. American Mathematical Soc., annual, Pittsburgh, Pa. (E. G. Begle, AMS, Yale University, New Haven, Conn.)

27–29. Arctic Inst. of North America, Berkeley, Calif. (R. C. Wallace, 4 Centre St., Kingston, Ont., Canada.)

27–29. Astronomical Soc. of the Pacific, Berkeley, Calif. (S. Einarsson, Leuschner Observatory, Univ. of California, Berkeley 4.)

27–29. International Conf. on Animal Venoms, Berkeley, Calif. (N. Porges, Eastern Regional Research Laboratory at Wyndmoor, Philadelphia, Pa.)

27–29. Soc. for Industrial and Applied Mathematics, 1st, Pittsburgh, Pa. (H. W. Kuhn, Dalton Hall, Bryn Mawr College, Bryn Mawr, Pa.)

27–29. Western Soc. of Naturalists, Berkeley, Calif. (J. L. Mohr, Univ. of Southern California, Los Angeles 7.)

27–30. Berkeley Symposium on Mathematical Statistics and Probability, 3rd, Berkeley, Calif. (J. Neyman, Dept. of Mathematics, Univ. of California, Berkeley 4.)

27–30. Econometric Soc., Detroit, Mich. (R. L. Cardwell, Cowles Commission, Univ. of Chicago, Chicago 37.)

27–30. National Assoc. of Biology Teachers, Berkeley, Calif. (P. Webster, Bryan City High School, Bryan, Ohio.)

27–30. Soc. of Systematic Zoology, Berkeley, Calif. (R. E. Blackwelder, U.S. National Museum, Washington 25.)

28–29. Linguistic Soc. of America, Detroit, Mich. (A. A. Hill, 1719 Massachusetts Ave., NW, Washington 6.)

28–29. Meteoritical Soc., Berkeley, Calif. (J. A. Russell, Univ. of Southern California, Los Angeles 7.)

28–29. Northwest Scientific Assoc., Missoula, Mont. (F. J. Schadegg, Eastern Washington College of Education, Cheney, Wash.)

28–30. American Economic Assoc., Detroit, Mich. (J. W. Bell, Dept. of Economics, Northwestern Univ., Evanston, Ill.)

28–30. American Meteorological Soc., Berkeley, Calif. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)

28–30. American Physical Soc., Berkeley, Calif. (J. Kaplan, Dept. of Physics, Univ. of California, Los Angeles 24.)

28–30. American Soc. of Limnology and Oceanography, Berkeley, Calif. (B. H. K. Ketchum, Woods Hole Oceanographic Institution, Woods Hole, Mass.)

Meetings & Conferences

December, *contd.*

28–30. American Soc. of Zoologists, Chapel Hill, N.C. (R. T. Kempton, Vassar College, Poughkeepsie, N.Y.)

28–30. Archaeological Inst. of America, annual, Boston, Mass. (C. G. Yavis, Andover Hall, Francis Ave., Cambridge 38, Mass.)

28–30. Gerontological Soc., annual, Gainesville, Fla. (N. W. Shock, Baltimore City Hospitals, Baltimore 24, Md.)

29. Assoc. for Symbolic Logic, Pittsburgh, Pa. (J. Barlaz, Rutgers Univ., New Brunswick, N.J.)

29–30. History of Science Soc., New York, N.Y. (M. Bons, Brandeis Univ., Waltham, Mass.)

30. Mathematical Assoc. of America, Pittsburgh, Pa. (H. M. Gehman, Univ. of Buffalo, Buffalo 14, N.Y.)

30. Soc. of General Physiologists, Berkeley, Calif. (J. B. Buck, National Institutes of Health, Bethesda 14, Md.)

January

2–8. Indian Science Congress Assoc., 42nd, Baroda, (ISCA, 1 Park St., Calcutta 16.)

11–14. American College of Surgeons, Inter-American session, Lima, Peru. (M. L. Mason, 40 E. Erie St., Chicago 11, Ill.)

11–14. Highway Research Board, Washington, D.C. (HRB, National Research Council, 2101 Constitution Ave., Washington 25.)

12. Astronomical Soc. of the Pacific, annual, San Francisco, Calif. (S. Einarsson, Leuschner Observatory, Univ. of California, Berkeley.)

12–15. World Symposium on Applied Solar Energy, Phoenix, Ariz. (M. L. Kastens, Stanford Research Inst., Stanford, Calif.)

13. American Genetic Assoc., annual business, Washington, D.C. (R. M. Cook, AGA, 1507 M St., NW, Washington.)

20–22. American Assoc. of Physics Teachers, New York, N.Y. (R. F. Paton, Dept. of Physics, Univ. of Illinois, Urbana.)

20–22. American Physical Soc., New York, N.Y. (K. K. Darrow, Columbia University, New York 27.)

21. Public Health Workshop on Dental Programs in Industry, 3rd, New York, N.Y. (A. J. Asgis, Hotel Statler, New York.)

24–27. American Soc. of Heating and Ventilating Engineers, Philadelphia, Pa. (A. V. Hutchinson, 62 Worth St., New York 13.)

26–2. Australian and New Zealand Assoc. for the Advancement of Science, Melbourne, Australia. (J. R. A. McMillan, 157 Gloucester St., Sydney.)

27. American Federation for Clinical Research, western section, Carmel, Calif. (A. B. French, College of Medicine, Univ. of Utah, Salt Lake City.)

28–29. Bur. of Biological Research, Rutgers Univ., New Brunswick, N.J. (W. H. Cole, College of Arts and Sciences, Rutgers Univ., New Brunswick.)

February

4–5. American Geophysical Union, Berkeley, Calif. (D. K. Todd, College of Engineering, Univ. of California, Berkeley 4.)

7–9. Conf. on Silicosis and Occupational Chest Diseases, Saranac Lake, N.Y. (N. R. Sturgis, Jr., Saranac Laboratory, Saranac Lake.)

7–11. American Soc. of Civil Engineers, San Diego, Calif. (W. N. Carey, 33 W. 39 St., New York 18.)

Meetings & Conferences

February, *contd.*

11–25. Pan American Acad. of General Practice, Lima, Peru. (A. Martinez, 54 E. 72 St., New York 21.)

13–17. American Inst. of Mining and Metallurgical Engineers, annual, Chicago, Ill. (E. H. Robie, 29 W. 39 St., New York 18.)

14–19. Latin American Cong. of Physical Medicine, Lima, Peru. (C. L. de Victoria, 176 E. 71 St., New York 21.)

17–19. American Acad. of Forensic Sciences, Los Angeles, Calif. (W. J. R. Camp, 1853 Polk St., Chicago 12, Ill.)

28–2. American Educational Research Assoc., St. Louis, Mo. (F. W. Hubbard, 1201 16 St., NW, Washington 6, D.C.)

March

2–4. American Assoc. of University Professors, Gatlinburg, Tenn. (R. E. Himstead, AAUP, 1785 Massachusetts Ave., NW, Washington 6, D.C.)

7–11. American Soc. of Photogrammetry, Washington, D.C. (C. E. Palmer, 1000 11 St., NW, Washington 1.)

7–11. National Assoc. of Corrosion Engineers, 11th annual, Chicago, Ill. (A. B. Campbell, 1061 M & M Bldg., Houston 2, Tex.

14. American Educational Research Assoc., Denver, Colo. (F. W. Hubbard, 1201 16 St., NW, Washington 6, D.C.)

14. Wildlife Soc., Montreal, Canada. (D. L. Leedy, Fish and Wildlife Service, Washington 25, D.C.)

17–19. American Physical Soc., Baltimore, Md. (K. K. Darrow, Columbia University, New York 27).

17–19. International Symposium on Cardiovascular Surgery, Detroit, Mich. (John Keyes, Henry Ford Hospital, Detroit 2.)

17–19. National Wildlife Federation, Montreal, Canada. (C. H. Callison, 232 Carroll St., NW, Washington 12.)

17–2. Inter-American Statistical Conf., 3rd, Santiago, Chile. (IASI, Pan American Union, Washington 6.)

20–23. American Assoc. of Dental Schools, annual, Chicago, Ill. (M. W. McCrea, 42 S. Greene St., Baltimore 1, Md.)

24–26. National Science Teachers Assoc., Cincinnati, Ohio. (R. H. Carleton, 1201 16 St., NW, Washington, D.C.)

28–31. American Assoc. of Petroleum Geologists, New York, N.Y. (E. H. Powers, Box 670, Fort Worth, Tex.)

28–1. Western Metal Exposition, 9th, Los Angeles, Calif. (W. H. Eisenman, 7301 Euclid Ave., Cleveland 3, Ohio.)

31–2. Soc. of Research in Child Development, Monticello, Ill. (C. B. Stendler, College of Education, Univ. of Illinois, Urbana.)

April

1–5. Japan Medical Cong., Kyoto. (M. Goto, Univ. Hospital, Kyoto Univ., Kyoto.)

2. Kappa Delta Pi, Cleveland, Ohio. (E. I. F. Williams, 238 E. Perry St., Tiffin, Ohio.)

3–6. American Astronomical Soc., Princeton, N.J. (C. M. Huffer, Washburn Observatory, Madison 6, Wis.)

3–7. American College Personnel Assoc., Chicago, Ill. (C. Evans, Univ. of Indiana, Bloomington.)

4. American Educational Research Assoc., Cleveland, Ohio. (F. W. Hubbard, 1201 16 St., NW, Washington, 6, D.C.)

4–6. American Assoc. of Physical Anthrolpologists, Philadelphia, Pa. (J. L. Angel, Jefferson Medical College, 307 S. 11 St., Philadelphia 7.)

Meetings & Conferences

April, ***contd.***

6–7. Kansas Acad. of Science, Lawrence. (C. T. Rogerson, Dept. of Botany, Kansas State College, Manhattan.)

6–8. American Assoc. of Anatomists, Philadelphia, Pa. (N. L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Ohio.)

9. South Carolina Acad. of Science, Columbia, S.C. (H. W. Freeman, Univ. of South Carolina, Columbia.)

10–15. American Inst. of Homeopathy, Washington, D.C. (W. R. Huntsman, AIH, 1601 Chestnut St., Philadelphia 3, Pa.)

10–15. American Inst. of Nutrition, San Francisco, Calif. R. W. Engel, Dept. of Biochemistry and Nutrition, Virginia Polytechnic Inst., Blacksburg.)

10–16. American Physiological Soc., San Francisco, Calif. (M. O. Lee, 2101 Constitution Ave., Washington 25.)

10–16. American Soc. for Experimental Biology, San Francisco, Calif. (C. C. Erickson, Inst. of Pathology, Univ. of Tennessee, 858 Madison Ave., Memphis.)

10–16. Federation of American Societies for Experimental Biology, San Francisco, Calif. (M. O. Lee, 2101 Constitution Ave., Washington 25, D.C.)

11–14. Assoc. of American Geographers, annual, Memphis, Tenn. (B. W. Adkinson, Library of Congress, Washington 25, D.C.)

11–15. American Assoc. of Immunologists, annual, San Francisco, Calif. (F. S. Cheever, Graduate School of Public Health, Univ. of Pittsburgh, Pittsburgh 13.)

11–15. American Soc. of Biological Chemists, San Francisco, Calif. (P. Handler, Duke Univ. School of Medicine, Durham, N.C.)

12–15. International Union of Biological Sciences, 12th general assembly, Rome, Italy. (P. Weiss, 2101 Constitution Ave., Washington 25, D.C.)

14. World Meteorological Organization, 2nd cong., Geneva, Switzerland. (G. Swoboda, WMO, 1, Ave. de la Paix, Geneva.)

14–16. National Speleological Soc., Natural Bridge, Va. (E. Moffett, 3047 S. Columbus St., Arlington, Va.)

15–16. American Mathematical Soc., Brooklyn, N.Y. (AMS, 80 Waterman St., Providence 6, R.I.)

15–16. Eastern Psychological Assoc., Philadelphia, Pa. (G. Lane, Dept. of Psychology, Univ. of Delaware, Newark.)

15–16. Iowa Acad. of Science, Davenport. (J. L. Laffoon, Iowa State College, Ames.)

18–19. National Air Pollution Symposium, 3rd, Pasadena, Calif. (A. M. Zarem, 621 S. Hope St., Los Angeles 17, Calif.)

21–22. Eastern States Health Education Conf., New York Academy of Medicine, New York, N.Y. (NYAM, 2 E. 103 St., New York 29.)

21–23. Assoc. of Southeastern Biologists, annual, Charleston, S. C. (M. E. Gaulden, Biology Div., Oak Ridge National Laboratory, Oak Ridge, Tenn.)

22–23. Arkansas Acad. of Science, annual, Searcy. (L. F. Bailey, Univ. of Arkansas, Fayetteville.)

22–23. Georgia Acad. of Science, Athens. (W. B. Redmond, Box 534, Emory University, Ga.)

24–26. American Association for the Advancement of Science, southwestern division, Sante Fe, N.M. (F. E. E. Germann, Dept. of Chemistry, Univ. of Colorado, Boulder.)

24–29. Inter-American Cong. of Radiology, Washington, D.C. (E. P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa.)

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Biochemist, Dr. Phil. Swiss, 36 years, all around practice in org., inorg., synthetic chemistry, leader of scientific department of Swiss pharmaceutical firm, knowledge in related fields of pharm. research work (bacteriology, pharmacology), experienced in erecting ampoule manufacturing department, coating department, teaching experience, wants new position (industrial or research department) in Europe or abroad. German, English, French, some Spanish. Box 275, SCIENCE. X

Botanist. (Taxonomy, Phytogeography, Bryophytes); B.S. (Univ. California); Ph.D. (Univ. Michigan); 15 publications; post-doctoral research fellow, 1950; interested teaching and research. Leo F. Koch, Visiting Assistant Professor, Tulane University, New Orleans. X

(a) Internist, Diplomate; scientific background, M.S.; four years, teaching and research; three years, director, research, pharmaceutical company. **(b) Parasitologist,** Ph.D.; well trained malariology and related protozoan diseases; three years on staff research institution. Medical Bureau (Burneice Larson, Director), Palmolive Building, Chicago. X

Pathologist. Certified Clinical and Anatomic Pathology. Age 38. Catagory IV. Associate professor. Extensive surgical pathology, teaching, research, publications. Desire hospital appointment with academic and research possibilities. Box 274, SCIENCE. 11/19,26;12/3

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Abstractor (female) to abstract medical journals—large ethical pharmaceutical company, Midwest. College graduate, Science Major, preferred. Reply Box No. 267, SCIENCE. 11/12, 19, 26

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Pharmacologist (Toxicologist)—Ph.D. or D.V.M. with training and experience in evaluating toxicity of potential new drugs. Background in pharmacodynamics desirable. Capacity to direct group activities essential. Send resumes to the Personnel Department, The Norwich Pharmacal Company, Norwich, New York. 11/12,19,26

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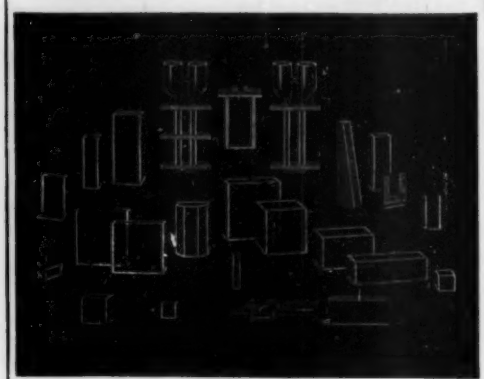

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